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COMPILATION OF ARTICLE SUMMARIES FROM ETS/IAQ REPORT

A Current Reference Document

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Collected From the Reports on Recent
ETS and IAQ Developments

SHB

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Please note: This document is not intended to be an encyclopedic summary of scientific literature relating to ETS. Rather, it only contains summaries and excerpts from those studies included in *Reports on Recent ETS and IAQ Developments.*

The summaries contained in this document are intended as a reference; the actual articles should be consulted for any purpose beyond a summary reference.

ENVIRONMENTAL TOBACCO SMOKE & INDOOR AIR QUALITY

ARTICLE SUMMARIES FROM CURRENT DEVELOPMENTS REPORTS

LUNG CANCER

[1] **Ger, L.-P., Hsu, W.-L., Chen, K.-T., and Chen, C.-J., "Risk Factors of Lung Cancer by Histological Category in Taiwan," *Anticancer Research* 13: 1491-1500, 1993 [Issue 65, Item 28]**

Although the authors of this study present data on "passive smoking," the study is *not* comparable to the spousal smoking studies on lung cancer, as the data are for smokers and nonsmokers *combined*, rather than for nonsmokers alone. The authors report a statistically significant risk of squamous or small cell carcinoma associated with ETS exposure from friends. Of the male squamous/small cell cases, 93.9 percent were themselves smokers.

EXCERPTS:

"The relationship between various risk factors and lung cancer by different histological types was evaluated in a case-control study. A total of 72 adenocarcinoma patients and 59 squamous/small cell lung cancer patients, 262 hospital controls and 262 neighborhood controls were interviewed."

"Table III shows little association between lung cancer and childhood and adult exposure to passive smoke. However, passive smoking exposure from spouse [OR = 2.84, 95% CI 1.04-7.78] and friends [OR = 2.28, 95% CI 1.03-5.05] was significantly associated with squamous/small cell carcinoma of the lung."

"[T]he use of coal as cooking fuel was significantly associated with squamous/small cell lung cancers, but not with the adenocarcinoma."

"Prior chronic bronchitis was related to squamous/small cell carcinomas of the lung, but not to the adenocarcinoma."

"There was a significant increase in odds ratios of developing adenocarcinomas of the lung for those employed as cooks, but no association with squamous/small cell carcinomas of the lung was observed."

"[D]ietary intake of vitamin A from plants was significantly different between cases of squamous/small cell carcinoma and their neighborhood controls only."

"It is difficult to assess passive smoking in interviews. Therefore, the relationship between passive smoking and lung cancer remains controversial in different epidemiological studies in Chinese populations."

"Most subjects who reported passive smoke exposure from friends were exposed while playing a Chinese game, mah-jong. Men who played mah-jong tended to close doors and windows to avoid transmitting any noise from playing mah-jong to neighbors. The intensity of passive smoke exposure from friends playing mah-jong was very strong under conditions of poor ventilation and for a long duration of three or more hours."

"[O]ur study found an inverse association between incense burning and lung cancer. This might be explained by the fact that the items on incense burning asked in our questionnaire could not estimate the exact exposure which the subjects underwent."

"In our study, no association between types of cooking and lung cancer was found, while those who had ever been employed as a cook had an increased risk of adenocarcinoma."

"[O]ur results suggest that associated risk factors for adenocarcinoma and squamous/small cell carcinoma of the lung are quite different. The most important risk factors for adenocarcinoma of the lung were asbestos-related jobs and working as a cook, while the most important risk factors for squamous/small cell carcinoma of the lung were active smoking, passive smoking exposure from friends, use of coal as cooking fuel, history of chronic lung diseases and asbestos-related jobs."

[2] **Mayne, S.T., Janerich, D.T., Greenwald, P., Chorost, S., Tucci, C., Zaman, M.B., Melamed, M.R., Kiely, M., and McKneally, M.F., "Dietary Beta Carotene and Lung Cancer Risk in U.S. Nonsmokers," *Journal of the National Cancer Institute* 86(1): 33-38, 1994 [Issue 64, Item 36]**

Another paper reporting the results of dietary analyses from a large case-control study of lung cancer in nonsmokers has been published. The authors of the study report that consumption of raw fruits and vegetables, vitamin E supplements, and dietary beta carotene are associated with a statistically significant reduction in nonsmoker lung cancer risk.

In contrast to the Alavanja, et al., paper the Mayne, et al., study does not include an investigation of fat consumption. *See* issue 61 of this Report, December 3, 1993. However, the authors note that whole milk consumption was associated with a statistically significant increase in risk, which they suggest might be related to the higher fat content in whole milk versus other varieties of milk.

The data reported in this paper are drawn from the Varela/Janerich case-control study of lung cancer in nonsmokers in New York. The Varela dissertation was completed in 1987; the data were published by Janerich, et al., in 1990, following the death of Dr. Varela.

EXCERPTS:

"To our knowledge, no studies to date have specifically examined the association between dietary factors and lung cancer risk in nonsmoking men. Consequently, we conducted this study to examine the association of dietary beta carotene with lung cancer risk in a relatively large number of nonsmoking men and women."

"A population-based, individually matched case-control study of lung cancer in nonsmokers was conducted in New York State from 1982 to 1985."

"To be included as a case subject in the study, a patient had to reside in the 23-county region, be between 20 and 80 years of age, never have smoked more than 100 cigarettes (nonsmoker), or have smoked at some time but not have smoked more than 100 cigarettes in the 10 years prior to diagnosis (former smoker)."

"With regard to confounding, several potential confounders (type of interview, smoking history, sex, county of residence, and age) were matched by design and thus were not included in the logistic models. Passive smoke exposure was quantified as previously described and was examined as a potential confounder by inclusion of the following summary variables in logistic models: household exposure during childhood and adolescence (<21 years of age), household exposure during adulthood, lifetime household exposure, smoker-years of exposure from a spouse, and pack-years of exposure from a spouse. None of the passive smoking variables were found to confound the dietary associations; thus, these variables were not included in the final models. The final multivariate models included the following potential confounders: body mass index, education, income, religion, and number of cigarettes smoked per day in former smokers. Use of cigars and pipes did not differ in case patients versus control subjects; thus, no adjustment was necessary for cigar/pipe use."

"Regarding the consumption of individual food items, case patients consumed significantly more whole milk and beer. Case patients, however, consumed significantly less of the following food items: tomatoes; greens (defined as all cooked greens and all salad greens except lettuce); fresh fruit other than peaches, apricots, or plums; skim or low-fat milk; cheeses, excluding ricotta, cottage, or cream cheese; and supplemental vitamin E."

"Consumption of greens, fresh fruit, and hard cheese was associated with a statistically significant dose-dependent reduction in risk, whereas consumption of whole milk was associated with a statistically significant, dose-dependent increase in risk for lung cancer."

"Ever use of vitamin E supplements was reported by 21.2% of the control subjects (86 of 406) versus 14.7% of the case patients (60 of 409). The OR for vitamin E supplements was 0.55 (95% confidence interval [CI] = 0.35-0.85) based on a case-control difference of 1 frequency unit/d."

"Subsequent analyses focusing on groups of related foods showed that increased consumption of the following food groups was associated with a statistically significant reduction in risk in females: vegetables, raw fruits and vegetables, and dairy products."

"In separate analyses, both raw fruits (adjusted OR = 0.64; 95% CI = 0.46-0.87) and raw vegetables (adjusted OR = 0.60; 95% CI = 0.38-0.95) were found to be significantly inversely associated with lung cancer risk."

"Beta carotene (OR = 0.70; 95% CI = 0.50-0.99), but not retinol (OR = 0.98; 95% CI = 0.82-1.17), was significantly inversely associated with lung cancer risk. . . . [T]he highest quartile of intake of beta carotene was associated with a significant reduction in risk relative to the lowest quartile of intake (adjusted OR = 0.54; 95% CI = 0.30-0.98; data not shown)."

"This is the largest study to date to examine the association between dietary factors and lung cancer risk in nonsmokers. Our results indicate that consumption of fruits and vegetables, especially those consumed raw, is associated with a reduced risk for lung cancer. The apparent protective effect of raw fruits and vegetables did not vary by type of interview, smoking history, sex, or age. The magnitude of the protective effect for fruits and vegetables was greatest for epidermoid carcinomas."

"Our results in this study suggest that fruits and vegetables typically consumed in a raw form confer greater protection than those typically processed in some manner. This observation could be explained by the fact that cooking has been shown to destroy carotenoids."

"The data suggest that dietary beta carotene, which is almost exclusively derived from the intake of fruits and vegetables, also reduced the risk of lung cancer (OR = 0.70; 95% CI = 0.50-0.99)."

"In the comparison of the consumption of individual food items by case patients and control subjects, a striking difference was found for milk consumption: Case patients consumed significantly more whole milk and significantly less skim or low-fat milk than their matched control subjects. The magnitude of the case-control difference in consumption of whole milk and skim or low-fat milk exceeded that of all other food items. . . . It is possible that the association between whole-milk consumption and lung cancer risk reflects an effect of dietary fat, since other studies have reported that dietary fat increases the risk of lung cancer. . . . The apparent protective effect of dairy products in women, but not in men, may reflect the fact that women consumed more cheese and skim or low-fat milk but less whole milk than men."

"The primary strengths of this study are the relatively large number of nonsmoking case patients studied, the inclusion of both males and females, and the population-based design. Also, efforts were made to identify and interview subjects rapidly, minimizing the need for surrogate respondents."

"A major limitation of this study, however, is that the questionnaire used did not inquire about the overall diet. Consequently, our data do not allow for an assessment of other dietary factors including high intake of fat and low intake of vitamin E as risk factors for lung cancer in nonsmokers."

"Our finding of an association between consumption of fruits and vegetables (especially raw fruits and vegetables) and of beta carotene and a reduced risk for lung cancer in nonsmokers suggests that public health efforts to increase the consumption of fruits and vegetables are likely to benefit both smokers and nonsmokers via a reduction in lung cancer risk. In addition, the apparent reduction in risk for lung cancer among vitamin E supplement users is a provocative finding and merits further examination."

[3] **Pershagen, G., Akerblom, G., Axelson, O., Clavensjo, B., Damber, L., Desai, G., Enflo, A., Lagarde, F., Mellander, H., Svartengren, M., and Swedjemark, G.A., "Residential Radon Exposure and Lung Cancer in Sweden,"** ***New England Journal of Medicine*** **330(3): 159-164, 1994 [Issue 65, Item 29]**

The data reported in this paper suggest that exposure to elevated levels of indoor radon over time is associated with a statistically significant increase in lung cancer risk. While the authors claim that active smoking and radon interact to increase cancer risk, they do not address ETS. Similarly, few of the spousal smoking studies of lung cancer have considered radon as a potential independent risk factor for lung cancer.

EXCERPTS:

"Residential radon is the principal source of exposure to ionizing radiation in most countries. To determine the implications for the risk of lung cancer, we performed a nationwide case-control study in Sweden."

"The study included 586 women and 774 men 35 to 74 years of age with lung cancer that was diagnosed between 1980 and 1984. For comparison, 1380 female and 1467 male controls were studied. Radon was measured in 8992 dwellings occupied by the study subjects at some time since 1947. Information on smoking habits and other risk factors for lung cancer was obtained from questionnaires."

"The primary aim of this study was to narrow the uncertainty in the estimation of the risk of residential exposure to radon, which necessitated a study considerably larger than any of the earlier investigations. A further aim to assess the interactions between residential radon exposure and other factors, primarily smoking."

"The radon levels in the 8992 homes where measurements were made followed an approximately log-normal distribution, with geometric and arithmetic means of 1.6 and 2.9 pCi per liter, respectively. The cutoff points for quartiles of radon levels were 0.8, 1.5, and 3.1 pCi per liter, and the highest measured concentration was 183 pCi per liter. [In the U.S., the EPA action level is 4 pCi per liter.]"

"The relative risks in subjects exposed to average time-weighted radon levels of 3.8 to 10.8 pCi per liter and to levels exceeding 10.8 pCi per liter were 1.3 (95 percent confidence interval, 1.1 to 1.6) and 1.8 (95 percent confidence interval, 1.1 to 2.9), respectively. The strongest association was suggested for small-cell carcinoma and adenocarcinoma."

"[C]urrent smokers exposed to an average of more than 10.8 pCi per liter had relative risks of 25 to 30. . . . The interaction between residential exposure to radon and smoking exceeded an additive effect."

"The interaction between residential radon and smoking with regard to lung cancer exceeded additivity and was more consistent with a multiplicative effect. This implies that the number of radon-related lung cancers in a population depends heavily on rates of smoking and that the reverse is also true -- i.e., the number of smoking-related cancers also depends on the level of radon exposure in the population."

"There is substantial uncertainty in the estimation of exposure to radon in the study subjects, which will primarily dilute the association with lung cancer."

[4] Letters to the Editor Regarding Rennie, D., "Smoke and Letters," *Journal of the American Medical Association* 270(14): 1742-1743, 1993 [Issue 67, Item 26]

In response to letters by tobacco industry personnel or consultants concerning the Trichopoulos, et al., autopsy study, Drummond Rennie, Deputy Editor (West) of the *Journal of the American Medical Association* (*JAMA*), wrote an editorial on the role of the editor in evaluating letters for publication. Further details on the study appear in issues 32 and 58 of this Report, October 9, 1992, and October 22, 1993. *JAMA* recently published a letter by Ronald M. Davis and Simon Chapman concerning Rennie's editorial and a reply from Rennie. The letters appear at 271(8): 583-584, 1994.

Davis and Chapman, respectively editor and deputy editor of the journal *Tobacco Control*, suggest that journal editors should treat letters as they would treat research papers. Namely, they suggest that "certain letters" should be sent to outside experts for peer review. Davis and Chapman suggest that candidate letters would be those that present new data or analyses, or those written by a "party with vested interests in the position being taken." While Davis and Chapman claim to agree with Rennie's position that journals should allow discussion of controversial issues, they go on to state that "many (or most) of the letters written, generated, or otherwise paid for by the tobacco industry are characterized by poorly informed, misleading, or downright silly arguments." They also suggest that "many (or most) of these correspondents are attempting to exploit scientific journals."

In his reply, Rennie opines that "[q]uality is hard to define." He suggests that even expert reviewers can "differ strenuously" on this issue. Rennie states that his decision to publish the letters from industry consultants or personnel did not mean that he was convinced by them or agreed with their arguments. He continues: "I did not endorse the letters, indeed, I was unimpressed by them, but I thought they were rational and of sufficient quality to publish." Rennie concludes with the observation that having the opportunity for review and rebuttal of every letter sent to the *JAMA* would be "ponderous, time-consuming, complicated, redundant, and crushing to criticism."

[5] Letters to the Editor Regarding Siegel, M., "Involuntary Smoking in the Restaurant Workplace: A Review of Employee Exposure and Health Effects," *Journal of the American Medical Association* 270(4): 490-493, 1993 [Issue 67, Item 27]

JAMA recently published two letters concerning a review by Siegel, which purported to show that ETS exposures were greater in restaurants than in homes, and that this correlated with an increased risk of lung cancer reported for waiters. *See* issue 53 of this Report, August 6, 1993, for the original article and an editorial. A letter by Gray Robertson in response to the Siegel claims, and a reply by Siegel were published. The letters appear at *JAMA* 271(8): 584-585, 1994.

Gray Robertson comments that Siegel's calculation of airborne nicotine concentrations, based on a literature review, "confirms the accuracy" of nicotine levels measured by Robertson and colleagues and presented at a tobacco-industry-sponsored press conference in 1988. He then describes the paper as claiming that since waiters reportedly have a 1.5 times higher probability of developing lung cancer and that ETS levels (based on nicotine) are about 1.6 times higher in restaurants than in homes, ETS "must be" related to the development of lung cancer. Robertson calls this "nonsense." He also questions Siegel's objectivity. Robertson comments that results reported by tobacco-industry-funded researchers are "accorded no credence," and suggests that when similar results are reported by a someone in public health and "given an alarmist spin," they are not questioned.

In his reply, Siegel states that Robertson's letter provides "valuable support" for his conclusion that ETS exposure is increased among restaurant workers. Siegel disagrees with Robertson's assessment of how he arrived at his conclusion, stating that he had reviewed "possible explanations" of the reported increased risk for lung cancer among food service workers, and concluded that ETS was the only "environmental exposure" that could account for the reported risk. Siegel also suggests that the "cigarette equivalent" approach to estimating nicotine exposure used by Robertson could be replaced by a new method for calculating "risk from involuntary smoking" using nicotine. Citing a recent paper by Repace and Lowrey, Siegel claims that ETS is associated with a seven in 1,000 lifetime risk of lung cancer. *See* issue 57 of this Report, October 8, 1993.

[6] **Thompson, D.H., and Warburton, D.M., "Dietary and Mental Health Differences Between Never-Smokers Living in Smoking and Non-Smoking Households,"** ***Journal of Smoking-Related Disorders*** **4(3): 203-211, 1993 [Issue 63, Item 27]**

This paper reports on an analysis of data from the Health and Lifestyle Survey, conducted in Great Britain and published in 1987. The authors report that non-smokers who lived with smokers were more likely to consume more saturated fats, fewer vegetables, and more alcohol than were nonsmokers who lived with smokers. In addition, those in smoking households also reported more depression and insomnia than did persons in nonsmoking households. The authors suggest that their analyses support the role of diet and lifestyle factors as confounders of the reported epidemiologic associations between ETS exposure and disease.

EXCERPTS:

"In this paper, we present some evidence of the confounding effect of diet on studies of the association of ETS with an increased risk of cancer and heart disease."

"In view of this fragmentary evidence that studies of the effects of ETS may be confounded by differences in lifestyle between ETS-exposed and non-smokers, who are not exposed to ETS, we investigated these differences with particular reference to diet, alcohol consumption and mental health of a large sample of never-smokers living in smoking and non-smoking households."

"Our results show important lifestyle differences between never-smokers living in smoking households (SH) and never-smokers living in non-smoking households (NSH). SH consume fats more frequently, drink more alcohol and eat fewer root vegetables and cereal. In addition, SH have poorer mental health than NSH. We now consider some of the health implications of these differences."

"Our results show that SH are more likely to consume chips, whole milk, butter, crisps, sausages and are more likely to fry their food than NSH. As a consequence, this group will be consuming a greater quantity of saturated fats."

"Our results show that SH are less likely to consume root vegetables (including carrots) and fresh fruit juice than NSH."

"The above results show a possible confounding effect of dietary carotene intake when studying the risk of developing lung cancer. Therefore, it is important to take into account studies which have shown a strong relationship between lung cancer risk and carotene intake. Whether dietary differences are sufficient to explain completely the reported increased relative risk of lung cancer in those exposed to tobacco smoke is unknown. However, it is true that nearly every study of ETS and disease has failed to take such dietary differences into account."

"If the data for alcohol consumption in the previous week are representative of typical consumption, there are a greater number of non-drinkers, heavier drinkers and fewer moderate drinkers in SH."

"Our results show that a greater proportion of SH never drink coffee while a slightly greater percentage drink over five cups per day. It is difficult to establish the health consequences for such differences in consumption."

"Our results show that SH were more likely to be experiencing insomnia or to report higher rates of depression than NSH. This conclusion is based on replies to the four questions: 'Face up to your problems?', 'Everything getting on top of you?', 'Unhappy and depressed?' and 'Losing confidence in yourself?'. In addition more of those in NSH had been 'Keeping busy and occupied?'"

"It is not possible to establish whether the respondents in the present study would have met diagnostic criteria for major depression. However, it seems clear that an individual's state of mind can have an important effect on physical well-being and so represents a negative health indicator for SH."

"There are a number of differences between never-smokers living in smoking and NSH which have adverse implications for health and are confounding factors in the study of the health consequences of ETS. Future studies of ETS and health should control for these factors. Also, from the database we are unable to determine the diet of children of the respondents."

"However, it would seem a reasonable assumption that children living in SH will have similar diets to the adults in the household and so a less healthy diet than children living in NSH. Given the association of poor diet and proneness to infection, it might be expected that there would be a higher incidence of infection among children living in SH."

CARDIOVASCULAR ISSUES

[1] **He, Y., Lam, T.H., Li, L.S., Li, L.S., Du, R.Y., Jia, G.L., Huang, J.Y., and Zheng, J.S., "Passive Smoking at Work as a Risk Factor for Coronary Heart Disease in Chinese Women Who Have Never Smoked," *British Medical Journal* 308: 380-384, 1994 [Issue 66, Item 24]**

In this case-control study of 59 nonsmoking Chinese women with coronary heart disease and 126 controls, the authors report that, after adjusting for a number of potential risk factors, risk estimates for spousal smoking and workplace smoking were *not* statistically significant. They do, however, claim that their data suggest increasing risk with increasing exposure at the workplace.

EXCERPTS:

"The present study is a second case-control study which aims to study whether passive smoking at work is a risk factor for coronary heart disease in women who have never smoked. It takes into account passive smoking from the husband and other risk factors."

"The cases were patients with coronary heart disease (non-fatal, incident cases) from the three large teaching hospitals of two medical universities in Xi'an . . . The final diagnosis was myocardial infarction . . . or coronary stenosis."

"A standardised questionnaire was designed to collect information on demographic characteristics (such as ethnic origin, age, residential history, educational level, occupation, and marital status); history of hypertension, hyperlipidaemia and diabetes mellitus; family history of hypertension, stroke, and coronary heart disease; history of smoking and passive smoking from husband and at work; drinking history; exercise; and psychosocial factors (such as Type A personality, experience of mental trauma, and stressful life events)."

"Physical examinations followed standard methods and included height, weight, body mass index, systolic and diastolic blood pressure, chest radiography, and electrocardiography. Laboratory investigations included serum concentrations of total cholesterol, triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol, and apolipoprotein A-1 and B and tests of liver and renal function."

"Passive smoking from husband was defined as living with a smoking husband for over five years. . . . Passive smoking at work was defined as working with smoking coworkers in the same office or factory unit for over five years."

"For passive smoking from husband, the crude odds ratio was 2.12 (1.06 to 4.25). . . . [T]he crude odds ratio for passive smoking at work was 2.45 (1.23 to 4.88)."

"The odds ratio for combined exposure to both sources, 4.18, was slightly higher than expected from the additive model but much less than expected from the multiplicative model. The crude odds ratio for any exposure (from husband or at work, or both) was 2.87 (1.28 to 6.55)."

"[T]he final model of logistic regression analysis . . . included passive smoking from husband and at work as the base . . . and age, history of hypertension, type A personality, and high density lipoprotein cholesterol concentration. . . . The adjusted odds ratio for passive smoking from husband was 1.24 (0.56 to 2.72) and at work was 1.85 (0.86 to 4.00). Both adjusted odds ratios were smaller than the respective crude ratios and became non-significant after the other five risk factors were included in the final model. When passive smoking was removed from the logistic model the adjusted odds ratio for passive smoking at work was slightly higher (1.92) but was still not significant. However, the adjusted odds ratio for any exposure (from husband or at work, or both) was significant (2.36; 1.01 to 5.55)."

"For passive smoking from husband, the crude odds ratios showed significant linear trends with amount smoked daily by husband, duration of exposure, and cumulative exposure (amount daily multiplied by duration), but the trends became non-significant after passive smoking at work and the other five risk factors were adjusted for in the final model. However, for passive smoking at work, . . . significant linear trends were found for the crude odds ratios in amount smoked daily, duration of exposure, number of smokers, exposure time daily, and cumulative exposure. For adjusted odds ratios, the linear trends were significant for all the variables except duration of exposure."

"To the best of our knowledge, this is the first study showing an increased risk of coronary heart disease with increasing exposure to passive smoking at work."

"Comparing the odds ratios for the two sources of environmental tobacco smoke, the crude and adjusted odds ratios for passive smoking at work were slightly greater than those for passive smoking from husband. If these were not due to chance, the higher risk for passive smoking at work may be explained by the fact that exposures to tobacco smoke at work are higher than exposures at home because the density of smokers is higher at work, and the length of stay at work for a working women is longer than the time she is exposed to

her husband's smoking at home. . . . Because the prevalence of smoking among men is high in China and most men smoke freely at home and at work, women are heavily exposed to environmental tobacco smoke and he magnitude of the risks could be quite high."

[2] **Mori, L., Bertanelli, F., Fabiano, P., Battaglia, A., and Leone, A., "Indoor Passive Smoking and Cardiac Performance: Mechanisms Able to Cause Heart Failure,"** ***Journal of Smoking-Related Disorders*** **4(3): 213-217, 1993 [Issue 63, Item 28]**

In this Italian study, male subjects exercised in a "smoke-free" environment, and in an environment where smoking took place. The authors report "impaired cardiac performance" in both "healthy" subjects, and in subjects who had previously had a myocardial infarction.

EXCERPTS:

"Nineteen non-smoking male volunteers -- nine healthy and 10 with a previous myocardial infarction, underwent exercise stress testing twice: once in a smoke-free environment and once in a smoking environment (carbon monoxide concentration 30-35 ppm)."

"In healthy people, we observed the following change after exercise in a smoking environment: mean prolonged time to recovery to pre-exercise heart rate [19 min vs. 8.5 min]. Survivors of infarction showed a significant reduction of the peak of exercise [80 watts vs. 120 watts], prolonged time to recovery to pre-exercise heart rate [21 min vs. 12.3 min], increased blood carbon monoxide concentration [2.3% vs. 1.2] and cardiac arrhythmias."

"The results obtained seemed to depend on environmental hypoxia due to carbon monoxide for healthy people and environmental hypoxia associated with increased post-exercise blood carbon monoxide concentration for survivors of infarction."

"Two main questions arise from the results of this study. First, the role of passive smoking as a factor for progressive cardiac damage, which is influenced by the degree and type of exposure to smoking. Second, the different pathological mechanism able to impair cardia function in healthy and diseased subjects."

"Heart disease has emerged as an important consequence of environmental tobacco smoke (ETS). There is epidemiological evidence that passive smoking may cause approximately a 30% increase in the risk of death due to heart disease. Moreover, ETS reduces exercise ability in ischaemic patients by up to 30%."

"Either acute or chronic exposure to passive smoking may damage the cardiovascular system. Chronic exposure may lead to ischaemic heart disease, whereas acute exposure impairs cardiac function, as our studies show. Moreover, cardiac impairment begins to be quite evident at low blood and environmental CO concentrations in survivors of acute myocardial infarction. This latter effect seems to depend on three factors: the environmental CO concentration, blood CO concentration and individual health."

"To our knowledge, no study closely links passive smoking and acute heart failure. . . . At present, the link between passive smoking and heart failure remains an area of doubt and intensive debate."

"Perhaps future studies should assess the effect of passive smoking on various aspects of cardiac pathology in patients who already suffer from some form of ischaemic heart disease."

RESPIRATORY DISEASES AND CONDITIONS -- ADULTS

[1] **Greer, J.R., Abbey, D.E., and Burchette, R.J., "Asthma Related to Occupational and Ambient Air Pollutants in Nonsmokers,"** ***Journal of Occupational Medicine*** **35(9): 909-915, 1993 [Issue 64, Item 37]**

A cohort of 3,914 California Seventh-Day Adventists was studied for this report on adult asthma. The authors claim that workplace ETS exposure was statistically significantly associated with asthma risk in their population, as was airway obstructive disease before age 16, and ozone exposure (in men only).

EXCERPTS:

"We attempted to determine the association between occupational and air pollutant exposure with the development of adult asthma through the analysis of a standardized respiratory questionnaire administered to a cohort of 3914 nonsmoking adults in 1977 and again in 1987. Ambient air pollution concentrations were estimated over a 20-year period using monthly interpolations from fixed-site monitoring stations applied to zip code locations by month of residence and work site."

"The variable 'Years Worked with a Smoker through 1987' (YWS87) contained a confidence interval that excludes one. Interestingly, 'Obstructive Airways Disease Before Age Sixteen' (AODB16) is significant with a relative risk (RR) of 4.24. Even though the relative risk (RR = 1.31) for mean ozone concentration exposure

through 1987 approaches statistical significance, the confidence interval does include one. The variables 'Years of Occupational Dust Exposure,' 'Years of Occupational Vapor Exposure,' 'Cumulative Occupational Asthmagenic Substance Exposure,' and ambient mean TSP concentration all failed to reach .10 level of significance."

"Further sex-specific analysis revealed a statistically significant relative risk for ozone in men of 3.12, but ozone was not significant at the .05 level in women. YWS87 and AODB16 remained significant in both genders, with relative risks of 1.46 and 7.01 for men and 1.50 and 3.36 for women, respectively."

"Due to the small number of incident cases of asthma (84) and the small number of people reporting exposures other than environmental tobacco smoke (ETS) (661, 16.9% of the population), the power for detecting a relative risk greater than 1.5 for asthmagenic occupational exposures is less than 50%. Thus we cannot conclude that a lack of statistical significance for other occupational exposures indicates a real lack of association."

"In this population, ETS in the workplace is associated with the development of adult-onset asthma in both men and women. In fact, it is consistently associated with each of the asthma outcomes considered. ETS was the strongest occupationally related predictor of new onset asthma. . . . Relative risks associated with ETS reported here are consistent with those reported elsewhere."

"Long-term exposure to ozone was strongly associated with adult-onset asthma in men (RR = 3.12) for a 1 part per hundred million (pphm) incremental annual increase in mean concentration but not in women (RR = .94) in this population."

"Interestingly, TSP, which has been implicated in the genesis of asthma in other studies, was not a significant factor in the presence of ozone in this population."

"In summary, workplace ETS is by far the most common preventable asthmagenic exposure in this population. This has practical public health implications due to the high prevalence of workplace ETS in this country. ETS is not as well recognized in the occupational setting as a potential respiratory irritant as many other less frequently encountered occupational exposures. A previous history of respiratory disease or symptoms strongly predicts the development of asthma. Common sense would suggest that these workers should avoid occupations associated with respiratory exposures including ETS and ambient air pollutants."

[2] Xu, X., and Wang, L., "Association of Indoor and Outdoor Particulate Level with Chronic Respiratory Illness," *American Review of Respiratory Disease* 148: 1516-1522, 1993 [Issue 68, Item 26]

Data collected in three areas of Beijing, China, are examined in this study. The authors report that indoor coal combustion was associated with increased respiratory symptoms in the persons studied. Data on "passive smoking" were reportedly collected, but were not discussed in the paper, except for a comment that they were adjusted for in certain analyses.

EXCERPTS:

"The effect of indoor and outdoor particulate level on respiratory health was examined in 1,576 never smokers, 40 to 69 yr of age residing in industrial, residential, and suburban areas. The health outcomes of interest in this report were physician-diagnosed bronchitis, asthma, and six respiratory symptoms including chronic cough, chronic phlegm, bouts of cough and phlegm, shortness of breath (SOB), wheeze, and wheeze with SOB. Households with coal stoves had substantially higher indoor particulate levels than those with gas stoves. Subjects were grouped into three exposure categories according to the indoor use of coal stoves for both cooking and heating (B), either cooking or heating (E), or neither (N). The adjusted odds ratios for chronic phlegm, bouts of cough and phlegm, wheeze, and wheeze with SOB were significantly higher in the B than in the N group; the odds ratios for chronic cough and SOB were also higher for B than N, although these were not significant. The odds ratios in the E group were significantly greater for wheeze with SOB than in the N group but not for the other symptoms. The global estimates of the odds ratios for the six symptoms were 1.4 and 2.0, respectively, for the E and B groups. The particulate level was highest in the industrial area and lowest in the suburban area. There was an excess risk of all respiratory symptoms among subjects residing in industrial and residential areas, with an increase in symptom prevalence with outdoor particulate levels. The estimated global odds ratio was 2.5 (95% confidence interval [CI]: 1.3 to 4.8) for a unit increase in particulate level. The association become [sic] undetectable when indoor coal combustion was removed from the regression model. The total particulate exposure, represented by the sum of indoor and outdoor particulate exposure scores, was significantly associated with increased prevalence of all the six symptoms. A similar trend was noted for bronchitis. However, particulate level showed no association with physician-diagnosed asthma."

"SO_2 emission results primarily from coal combustion, which is estimated at about 18 million tons each year. Nearly half of the coal consumed is burned in the cities, in small boilers and household stoves for heating and cooking. It is burned with low thermal efficiency, no desulfurization, inefficient dust collection, and low or no smokestacks. The particle mass in coal smoke is 90% or more inhalable. Although indoor coal combustion is the predominant source for indoor particulate, the outdoor particulate concentration also affects indoor level depending on the difference between indoor and outdoor concentrations and house ventilation. In addition, house dust may be picked up by indoor particulate monitors."

Respiratory Diseases and Conditions -- Children

[1] **Duff, A.L., Pomeranz, E.S., Gelber, L.E., Price, G.W., Farris, H., Hayden, F.G., Platts-Mills, T.A.E., and Heymann, P.W., "Risk Factors for Acute Wheezing in Infants and Children: Viruses, Passive Smoke, and IgE Antibodies to Inhalant Allergens," *Pediatrics* 92(4): 535-540, 1993 [Issue 64, Item 38]**

The authors of this study report that viral respiratory tract infections (particularly due to respiratory syncytial virus) are important risk factors for wheezing in children under the age of two, whereas viral infections (mostly rhinovirus) and sensitization to allergens are important risk factors in older children. They also claim that ETS exposure, as determined by cotinine levels, was common among all wheezing children in the study, but that high cotinine levels were "significantly more common" among children less than two years of age.

EXCERPTS:

"The purpose of the present study was to examine the relationship of sensitization to inhaled allergens, viral infection, and passive smoke exposure in a nonselected population of infants and children treated for wheezing in a pediatric emergency department. An additional objective was to determine at what age IgE antibody to inhalant allergens in these children can be demonstrated as a risk factor for wheezing."

"Among wheezing patients under age 2, IgE antibody to inhaled allergens was uncommon. This finding is consistent with prospective studies of infants born to allergic parents . . . In our study, none of the young wheezing patients younger than 2 years of age had signs or symptoms of atopic dermatitis."

"An increased prevalence of IgE antibody to inhalant allergens was evident in wheezing patients after age 2 years, and a significant association between wheezing and sensitization was observed after age 4 years."

"Altogether, viral infections put children both less than and more than the age of 2 at significant risk for wheezing. . . . Our data from wheezing patients less than 2 years of age support the importance of RSV as a major respiratory pathogen for wheezing in infants. None of the virus-infected children less than age 2, however, had IgE antibody to inhaled allergens."

"The prevalence of tobacco smoke exposure at home was high for wheezing and control patients. Before the age of 2, however, a larger proportion of wheezing patients than controls were exposed to tobacco smoke. Studies of smoking trends in the United States indicate that rates of cigarette smoking are higher among lower socioeconomic groups. Consistent with this, the income status of our patients, judged by the proportion of the emergency department bill charged to parents, was lower for the wheezing children less than age 2 than for controls. Similarly, the income status for all smoke-exposed patients was lower than for nonexposed patients."

"The most striking finding regarding passive smoke exposure was the large proportion of children less than age 2 years who had elevated cotinine levels suggestive of heavy smoked exposure. . . . [W]e speculate that infants and young children, who are likely to be more physically dependent on their parents, may have a higher risk for heavy exposure if their parents smoke. However, a threshold level at which passive smoke exposure becomes clinically significant in causing or aggravating airway hyperresponsiveness has not yet been defined. In addition, when combined with other risk factors, the effects of smoke inhalation may be additive so that lower levels of exposure may have adverse consequences even for older children."

[2] **Forastiere, F., Agabiti, N., Corbo, G.M., Pistelli, R., Dell'Orco, V., Ciappi G., and Perucci, C.A., "Passive Smoking as a Determinant of Bronchial Responsiveness in Children," *American Journal of Respiratory and Critical Care Medicine* 149: 365-370, 1994 [Issue 67, Item 28]**

These Italian researchers report that bronchial responsiveness was affected in children (particularly girls) exposed to high levels of ETS at home. They suggest that their data support an association between ETS exposure and the development of asthma.

EXCERPTS:

"The present study was . . . designed to clarify the effects of parental smoking on the degree of nonspecific bronchial responsiveness in children; factors that may reflect the child's level of exposure to environmental tobacco smoke were also considered."

"There were 825 children exposed to any parental smoke; in this group, in 14.4% only the mother smoked, in 49.0% only the father smoked, and in 36.6% both were smokers. . . . A low level of father's education was more prevalent among the group of subjects exposed to parental smoking, but no other differences were noteworthy."

"As in the larger data set, in the subsample maternal smoking was related to increased risk of asthma (OR 1.48, 95% CI 0.84 to 2.65) and cough or phlegm (OR 1.75, 95% CI 0.87 to 3.56), even though in this case the associations were not statistically significant. Sex-, height-, and age-adjusted FEV_1 and FEF_{25-75} were lower among subjects with passive smoking exposure in comparison with nonexposed individuals."

"In boys, there was no statistically significant increased risk in the categories studied, even though nonsignificant elevated odds ratios were found for both maternal and paternal smoking among those living in high-density households."

"For girls, both maternal and paternal smoking had a deleterious effect; statistically significant higher odds ratios were found for all responders (any smokers, OR 1.50; maternal smoking, OR 1.58) and for strong responders (any smokers, OR 2.70; maternal smoking, OR 2.92; paternal smoking, OR 2.59)."

"Gender, however, appears to modify the effect of passive smoking on BR in our study. Females had a greater frequency of response to methacholine than males when exposed to parental smoking."

"The simplest explanation for our results in girls is that they spend more time at home and are more exposed. An alternative possibility is that girls are more susceptible."

"The mechanism by which passive smoking can affect BR is unclear. Side-stream tobacco smoke, because of its complex chemical nature, may elicit an irritant effect involving parasympathetic receptors and a local inflammatory response of the bronchial tree, thus directly increasing BR; however, other pathways have been hypothesized."

"In conclusion, we suggest that the effects of parental smoking on children's BR are detectable when the conditions for a higher exposure level at home are met. Females seem to be more susceptible. The findings reinforce the evidence of an association between passive smoking and inception of bronchial asthma."

[3] Frischer, T., Kuhr, J., Meinert, R., Karmaus, W., and Urbanek, R., "Influence of Maternal Smoking on Variability of Peak Expiratory Flow Rate in School Children," *Chest* 104(4): 1133-1137, 1993 [Issue 64, Item 39]

Based on a cohort study of over 1,200 German children, the authors report that variability in a measure of lung function was related to maternal smoking. They claim that this finding suggests that maternal smoking contributes to the development of childhood asthma.

EXCERPTS:

"Determination of the variability of the peak expiratory flow rate (PEFR) by serial measurements of PEFR has been proposed as a simple and useful screening method for asthma in population-based studies. The variability of the PEFR is highly correlated with nonspecific bronchial hyperresponsiveness. We measured the variability of the PEFR in a population-based sample of 1,237 children aged 7 years, in order to study the relationship between the variability of the PEFR and exposure to maternal smoking."

"This report is based on a longitudinal cohort study of the natural history of asthma and allergies in childhood currently being conducted in southwestern Germany."

"An association between baseline pulmonary function and maternal smoking status was not observed."

"Children with respiratory symptoms during the week demonstrated increased diurnal PEFR variability more often than healthy children."

"The incidences of variables of interest in tertiles of PEFR variability are shown. Current maternal smoking was significantly more frequent in the highest tertile. There was also a nonsignificant trend for paternal smoking. The number of smoking parents in the household was significantly related to PEFR variability."

"For nonasthmatic children, maternal smoking was associated with a 13.7 percent higher PEFR variability (CI, 2.8 to 24.7 percent). For asthmatic children without atopy, PEFR variability was 54.7 percent higher (CI, 5.5 to 226.8 percent), whereas in atopic asthmatic children, PEFR variability was -8.5 percent (CI, -41.2 to 42.3 percent) lower when maternal smoking was reported."

"To the best of our knowledge, we demonstrated for the first time that maternal smoking can substantially increase the variability of the PEFR in school children."

"In our analyses, for the subgroup of asthmatic children (but not for nonasthmatic children), a negative interaction between maternal smoking and atopy was significant, suggesting that while both risk factors are associated with increased PEFR variability, their combination is not. This would tempt one to believe that there is no effect of maternal smoking on PEFR variability in atopic asthmatic children."

"Our data suggest that both atopy and maternal smoking can increase PEFR variability among asthmatic children but do not act independently, since the proportion of children being exposed to passive smoke decreases with increasing severity of the atopic disease. Negative findings in the literature regarding the impact of maternal smoking on respiratory health of children might be explained by such an effect."

"The mechanism by which passive smoking might increase bronchial responsiveness is still unclear."

"The assessment of exposure to passive smoke was fairly crude in our study, possibly leading to an underestimation of harmful effects. Nevertheless, our findings support the hypothesis that maternal smoking contributes to increased PEFR variability and thus to the development of asthma in childhood."

[4] **Jin, C., and Rossignol, A.M., "Effects of Passive Smoking on Respiratory Illness from Birth to Age Eighteen Months, in Shanghai, People's Republic of China," *Journal of Pediatrics* 123: 553-558, 1993 [Issue 63, Item 29]**

Respiratory illness among children in one district of Shanghai was discussed in this paper. The sample consisted of families in which the mother reportedly did not smoke; ETS exposure was approximated as the number of cigarettes smoked daily by other family members. The authors claim to find a dose-response relationship between numbers of cigarettes smoked by household members and the child's risk of respiratory illness.

EXCERPTS:

"The objective of this study was to evaluate the effects of household environmental tobacco smoke, in the absence of maternal smoking during pregnancy, on the cumulative incidence ('risk') of hospitalization for respiratory illness in infants from birth to age 18 months, with the use of data from a census of children residing in Shanghai, People's Republic of China."

"This study identified a significant dose-response relationship between daily household cigarette use and the cumulative incidence of respiratory illness in children from birth through age 18 months. This relation could not be explained by in utero effects of maternal smoking nor by any of the potential confounding factors evaluated. Being fed human milk for at least 1 month was identified as a preventive factor for respiratory illness and was independent of the effects of household cigarette use or number of household members. The latter variable, however, was relatively constant among the households studied. The effect of the failure to breast-feed an infant was estimated to be approximately equal to the effect of exposing an infant to household use of 10 to 19 cigarettes per day."

"The present study showed a gender difference in the 18-month cumulative of respiratory illness: boys appeared to be more affected than were girls."

"In Shanghai, the indoor air quality for households using coal stoves has been reported to be worse than the air quality for households using gas stoves. In our study, however, children living in households using coal stoves had a lower cumulative incidence of respiratory disease than did children from households using gas stoves. One possible contributing explanation for this result is that children spend most of their time in the parents' bedroom, where the fathers smoke, where as the cooking stove is located in the kitchen."

"Two potential sources of error in this study warrant discussion. The first is that exposure to passive smoke is not an easily quantifiable variable. Most studies of long-term health consequences of passive smoking have relied on the smoking status of parents or their household members as the basis for defining exposure status. In our study, the exact number of cigarettes smoked at home by each family member was difficult to ascertain accurately. . . . . Most of the smokers in this study were the children's fathers, who left their homes for their places of employment during workdays; the remainder were grandfathers and uncles who lived in the same household."

"The second potential source of error is recall bias. . . . In our study, however, this type of recall bias did not appear to be a substantial problem, because there was little difference in the number of episodes of respiratory illness reported per person by different respondents."

"This study demonstrated significant negative effects of household smoking on the respiratory health of Shanghai infants. Since the data were collected in 1985, the economy and lifestyle in China have changed substan-

tially because of the 'open door' policy. Smoking in young women is becoming fashionable, but the prevalence of smoking in male adults is stable at more than 70%. Under these circumstances, the public health effects of passive smoke on children's respiratory health documented in this study probably underestimate the current effects."

[5] **Joad, J.P., Pinkerton, K.E., and Bric, J.M., "Effects of Sidestream Smoke Exposure and Age on Pulmonary Function and Airway Reactivity in Developing Rats,"** ***Pediatric Pulmonology*** **16: 281-288, 1993 [Issue 68, Item 27]**

This study reports on an attempt to develop an animal model for the reported effects of ETS exposure on children: airway obstruction and nonspecific airway reactivity. The authors report that exposure of young rats to ETS did not produce the results expected.

EXCERPTS:

"This study was designed to determine if exposing the developing rat to sidestream smoke (SSS, a component of ETS) could function as a model for studying the effects of ETS exposure on children in the absence of in utero exposure to smoke. Specifically, this study was designed to determine if SSS exposure to the developing rat (1) causes airway obstruction and airway hyperreactivity to methacholine and/or serotonin, and (2) if these effects are dependent on age and/or chronicity of exposure."

"The major findings of this study are (1) chronic exposure of the developing rat to SSS did not alter body growth, lung weight/body weight ratio, R_L [pulmonary resistance], C_{Ldyn} [dynamic lung compliance], P_{PA} [pulmonary artery pressure], or airway reactivity to methacholine. However, chronic SSS exposure reduced airway reactivity, but not pulmonary artery reactivity to serotonin; (2) acute (3 hr, 4 day) exposures of the rat to SSS also did not alter body weight, lung weight/body weight ratio, R_L, C_{Ldyn}, or airway reactivity to methacholine; (3) regardless of exposure, younger rats showed greater relative lung weight and airway reactivity to methacholine than older rats."

"The epidemiologic data suggested that children raised in homes of smokers showed airway obstruction and increased airway reactivity. Thus, we expected that the rats chronically exposed to SSS in this study would have decreased lung function and increased airway reactivity to methacholine which they did not. There are several possible explanations for this."

"The first explanation may be that the animals received an insufficient concentration of SSS to mimic human exposures. The concentration of SSS that was used in this study was in the high relevant range for human exposures (RSP = 1 mg/m^3 and CO = 6.45 ppm). A very smoky, poorly ventilated room has an RSP of 1 mg/m^3. . . . [A] more usual home environment concentration is 0.02 to 0.2 mg/m^3."

"A second explanation may be that the SSS used in this study does not mimic ETS closely enough. . . . Since we were unable to mimic the portion of ETS which represents exhaled mainstream smoke, the rats may have not received the appropriate concentration of an important component of ETS."

"A third explanation may be that the mechanism by which the ETS causes lung problems in children may not be present in the Sprague Dawley rat."

"A final possible explanation is that perhaps intrauterine exposure to smoke is more important than extrauterine exposure in inducing lung changes."

"In conclusion, rats exposed postnatally to SSS did not appear to develop the effects reported in children raised in the homes of smokers: airway obstruction and increase nonspecific airway reactivity."

[6] **Lewis, S., Richards, D., Butler, N., Bynner, J., and Britton, J., "Effect of Factors Operating in Pregnancy and Early Childhood on the Occurrence of Wheezing up to Age 16,"** ***Thorax*** **48: 1055, 1993 [Issue 65, Item 30]**

The authors of this abstract, presented at the British Thoracic Society's summer meeting, claim that maternal smoking is an important risk factor for wheezing. They propose that associations with socioeconomic status, maternal age, and breast feeding are due to confounding effects of maternal smoking in pregnancy.

Exerpts:

"Maternal smoking during pregnancy and in early childhood, low birth weight, premature birth, low maternal age, and cessation of breast feeding have all been implicated in the aetiology of wheezing in childhood. . . . We have estimated the relative independent importance of these effects on the occurrence of wheezing up to 16 in 15712 subjects from a British national birth cohort of children . . . Univariate comparisons of prevalence revealed an association with maternal smoking, both during pregnancy and in the first five years of childhood, low social index, a birth weight of less than 2000 g, low

maternal age, and absence of breast feeding, and showed that social index, birth weight, maternal age, and breast feeding were all significantly associated with maternal smoking, both during and after pregnancy. In a multivariate regression, wheezing was most closely related to maternal smoking in pregnancy in a dose response manner (adjusted OR for 15+ cigarettes/day = 1.330, 95% CI 1.182-1.496), and independently related to low birth weight (adjusted OR for birth weight <2000 g = 1.362, 95% CI 1.001-1.853). After adjustment for maternal smoking in pregnancy and birth weight, there was no additional significant effect of social index, maternal age, or breast feeding, indicating that the univariate associations with these variables arose from confounding by maternal smoking. These data show that maternal smoking in pregnancy and low birth weight are the major independent predictors of childhood wheezing."

[7] **Roorda, R.J., Gerritsen, J., Van Aalderen, W.M.C., Schouten, J.P., Veltman, J.C., Weiss, S.T., and Knol, K., "Risk Factors for the Persistence of Respiratory Symptoms in Childhood Asthma,"** ***American Review of Respiratory Disease*** **148: 1490-1495, 1993 [Issue 65, Item 31]**

This Dutch study compared characteristics of childhood asthma with the persistence of respiratory symptoms during adulthood. The authors report that symptoms during adulthood were correlated with childhood symptoms, female sex, and airway responsiveness in childhood. ETS is only mentioned in one table, where the authors present risk estimates for adult symptoms for a number of variables, including "passive smoking in childhood." The risk estimates for this variable are all less than 1.0, although not statistically significantly so.

EXCERPTS:

"We have prospectively studied a group of asthmatic subjects initially seen in childhood and followed in young adulthood, focusing on the influence of several putative childhood risk factors on the persistence of respiratory symptoms in adulthood. The aim of this study was to elucidate the contribution of the respiratory symptom score, level of pulmonary function, and degree of airway responsiveness in childhood to the presence and severity of respiratory symptoms in adulthood. The influence of related factors such as age at onset of respiratory symptoms and duration of symptoms in childhood was also assessed."

"The median respiratory symptom score in childhood was significantly lower for subjects without symptoms in adulthood. Moreover, the rate of occurrence of each of the four major categories of symptoms was lower in subjects without symptoms in adulthood; for wheezing, this difference reached the level of statistical significance."

"For subjects symptomatic in adulthood, the respiratory symptom score had significantly decreased from that during childhood."

"For both groups, the level of pulmonary function improved between childhood and adulthood."

"The rate of occurrence of respiratory symptoms in adulthood was significantly higher for women, and it was significantly influenced by symptom score in childhood. Female sex also predicted symptom severity in adulthood."

"In summary, our study demonstrated the following important findings. First, respiratory symptoms persisted or recurred during young adulthood in a majority of subjects (76%). Second, the prognosis of childhood asthma in female patients was less favorable than in male patients."

"Both a higher prevalence of individual respiratory symptoms in childhood and a higher overall symptom score were found to predict the presence of symptoms in adults."

"It would appear that for subjects with moderate to severe asthma in childhood, the bulk will continue to have symptoms in adulthood. Important predictors of these adult symptoms include symptoms in childhood, female sex, and increased airway responsiveness in childhood."

"The prevalence of cigarette smoking was disturbingly high; however, no negative effects of cigarette smoking on health have yet been documented in our study population. Because the majority of subjects remained symptomatic as adults, the need for proper medical supervision of this population is clear."

[8] **Rylander, R., Pershagen, G., Eriksson, M., and Nordvall, L., "Parental Smoking and Other Risk Factors for Wheezing Bronchitis in Children,"** ***European Journal of Epidemiology*** **9: 517-526, 1993 [Issue 68, Item 28]**

This study reports statistically significant associations between a number of indices of parental smoking and wheezing bronchitis in children. The authors also report that parental atopy, recurrent upper respiratory tract

winter and spring for a population sample of schoolchildren. Herein, we present the results of cross-sectional and longitudinal analyses of these measurements and discuss the relationship between bronchial responsiveness to distilled water and atopy."

"In . . . models of the first measure of bronchial responsiveness (recorded in winter or spring), increased responsiveness was significantly associated with decreased FEF_{50}, FEF_{50}/FVC, and FEF_{75}/FVC. Bronchial responsiveness was also increased with respiratory disease and atopy. For winter measurements, younger age and recent respiratory illness were associated with greater responsiveness to distilled-water challenge. Male gender and presence of mother's smoking were significantly associated with bronchial responsiveness in the spring measurements."

"For . . . models of the change in bronchial responsiveness between winter and spring, atopy and FEF_{25} were found to be significant predictors. Maternal smoking and asthma were of borderline significance. . . . The regression coefficients for level of mother's smoking as a predictor of between-season change demonstrated a dose-response-like relationship; however, only the group with the highest level of exposure was significantly different from the group living with nonsmoking mothers. Hence, as with atopy, exposure to mother's smoking was associated with increased bronchial responsiveness only in the spring."

"Passive exposure to tobacco smoke has been found to be associated with increased levels of bronchial responsiveness in both nonasthmatic and asthmatic subjects. In our study we documented a borderline significant effect of maternal smoking on bronchial responsiveness in spring but not in winter; we also found that maternal smoking affected the change in response between surveys. When maternal smoking was analyzed as a four-category variable, only children whose mothers reported consumption of > 10 cigarettes per day demonstrated significantly greater responsiveness than unexposed children. The same level of maternal smoking has previously been identified as a risk factor for childhood asthma."

"A surprising finding was the effect of maternal smoking in the spring, when indoor ventilation rates would be expected to be higher and the level of indoor exposure to tobacco smoke lower. This effect may be related to an interaction of the effects of atopy and those of smoking, which has been described in another cross-sectional study. The finding of increased responsiveness is consistent with the known immunologic effects of cigarette smoking. Exposure to cigarette smoke may also heighten exposure to allergens by increasing the permeability of the airway epithelium. Thus, exposure to cigarette smoke is hypothesized to affect bronchial responsiveness only when the level of concurrent exposure to pollen is high and bronchial inflammation is more pronounced."

"In summary, we report a seasonal dependency of distilled water-induced airways responsiveness for a population sample of children. The degree of bronchial responsiveness increased for asthmatic children and for children reporting shortness of breath, but seasonal change was most closely associated with a skin test indicating atopy and specific allergy to grass pollen. Given that the increase in bronchial responsiveness to distilled water parallelled the seasonal increase in exposure to these allergens in atopic children, the physiologic basis linking atopy and airway response should be further explored."

[10] Weiss, S.T., "Environmental Tobacco Smoke and Asthma," *Chest* 104(4): 991-992, 1993 [Issue 64, Item 40]

In this editorial published with the Frischer, et al., study of variability of lung function measurements in children, the author claims that maternal smoking is an important factor in the incidence and severity of childhood asthma.

EXCERPTS:

"The article by Frischer et al on maternal smoking and peak flow variability in this issue of *Chest* is notable both for its subject matter and its methods."

"The ability of Frischer and coworkers to demonstrate significant correlations of peak flow variability with maternal smoking is likely to stimulate further research on peak flow monitoring as an important area of asthma investigation."

"With regard to results, the association of maternal cigarette smoking with peak flow variability demonstrated by Frischer et al highlights the importance of maternal cigarette smoking in relation to asthma incidence and severity."

"[T]here is no question that maternal cigarette smoking is an important exacerbating factor in established disease."

"Three things remain unclear: Does maternal cigarette smoking influence the development of asthma? What is the relative importance of pre- versus post-natal exposure? What is the mechanism by which maternal smoking exerts its effects?"

"In considering mechanisms and susceptible subgroups, the data are conflicting, at best. . . . Frischer and coworkers support a nonatopic mechanism, as their positive association was confined to nonatopic subjects."

infections, and breast feeding for less than three months were risk factors for this condition.

EXCERPTS:

"The aim of this study was to analyze the etiologic role of a number of risk factors for severe wheezing bronchitis in children, with particular emphasis on parental smoking and on interactions."

"The incidence of wheezing was higher in boys than in girls (RR = 2.6, 95% CI 1.8 - 3.7). There was an increased risk of wheezing bronchitis in children whose gestational age was 34 weeks or lower. Breast-feeding for more than three months reduced the relative risk for wheezing to 0.7 (95% CI 0.5 - 0.9). A high number of upper respiratory tract infections before 18 months of age increased the risk of hospitalisation for wheezing, especially among the youngest children. There were no differences in length or weight between cases and controls in the different age groups."

"Hereditary factors were of importance for wheezing in the children. Parental atopic disease increased the risk for wheezing primarily in the older children (RR = 1.7, 95% CI 1.0 - 3.0). When parental asthma was used to increase specificity for pulmonary disease, the relative risk increased to 2.2 (95% CI 1.4 - 3.6). Paternal asthma seemed to be a more important risk factor than maternal asthma, and the effects of parental asthma appeared stronger in boys than in girls. Atopic symptoms in first degree relatives, which also includes siblings, was associated with relative risk of 2.0 (95% CI 1.2 - 3.3)."

"If a pet had been kept at any time after the child's birth, the risk of wheezing was increased among the youngest children (RR = 1.8, 95% CI 1.1 - 3.0). Having a caged bird was the only type of pet showing a clear increase in risk. . . . The presence of a wall-to-wall carpet in the house covering more than 25 percent of the living area was associated with an increased risk for wheezing among the elder children."

"The relative risk for wheezing bronchitis if either or both of the parents smoked was 1.8 (95% CI 1.3 - 2.6)."

"The influence of maternal smoking was greater than that of paternal. There was a positive exposure-response relation. . . . The association between parental smoking and wheezing appeared strongest in the youngest group, which showed a relative risk of 2.6 (95% CI 1.4 - 4.8) when the mother smoked more than 10 cigarettes a day."

"There was a suggested increase in relative risk in children of mothers who smoked only during pregnancy (RR = 1.2, 95% CI 0.5 - 2.9), as well as in the group where the mother smoked only after the birth of the child (RR = 1.4, 95% CI 0.6 - 3.5). However, a clear increase in risk was found only in children of mothers who smoked during pregnancy and continued to smoke thereafter (RR = 1.9, 95% CI 1.3 - 2.8)."

"Combinations of the risk factors appeared to result in particularly high risks in the youngest age group, with relative risks of 4.6, 3.3 and 8.8 for parental smoking together with parental asthma, pets in the household and recurrent upper respiratory tract infections, respectively."

"This study confirms the importance of heredity and atopic disposition as risk factors for wheezing bronchitis in children."

"The important role of parental smoking as a risk factor for wheezing bronchitis in small children is confirmed in this study. . . . Underreporting of smoking, particularly among the control parents, has to be considered in the interpretation of these findings. The smoking habits among the mothers in the control group correspond well to smoking rates among women of similar age groups in other Swedish studies, indicating that underreporting of smoking was not a major problem. On the other hand, basing the exposure classification solely on parental smoking will result in some nondifferential misclassification, tending to dilute the association to environmental tobacco smoke."

"Socioeconomic factors such as education, ethnic background, housing conditions and early day-care attendance, did not show any correlation with wheezing in our study."

[9] Studnicka, M.J., Frischer, T., Weiss, S.T., Dockery, D.W., Speizer, F.E., and Neumann, M.G., "Seasonal and Allergenic Predictors of Bronchial Responsiveness to Distilled Water," *American Review of Respiratory Disease* 148: 1460-1466, 1993 [Issue 68, Item 29]

The authors of this study conducted in Austria report seasonal variation in airways responsiveness of children, related to atopy and allergy. Maternal smoking was also reportedly of borderline statistical significance as a predictor of bronchial responsiveness.

EXCERPTS:

"In this study, a recently developed single-step distilled-water protocol that was well tolerated by children was used to obtain repeated measurements of bronchial responsiveness over a 3-yr period. To test the hypothesis that seasonal change in bronchial responsiveness occurs, we completed bronchial challenge tests in

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"[T]here is a growing body of evidence suggesting that maternal cigarette smoking, either *in utero* or during the first year of life, is associated with the development of asthma."

"The gradual, but significant, increase in childhood asthma prevalence and hospitalization in the United States coincides with a doubling of cigarette smoking rates among women of child-bearing age in this country. Roughly 50 percent of all children under the age of 5 years are exposed to cigarette smoking either pre- or postnatally. We need to determine the role of maternal smoking in the onset of childhood asthma, and further research is clearly needed to accomplish this goal."

OTHER CANCER

[1] McCredie, M., Maisonneuve, P., and Boyle, P., "Antenatal Risk Factors for Malignant Brain Tumours in New South Wales Children," *International Journal of Cancer* 56: 6-10, 1994 [Issue 68, Item 30]

The authors of this Australian study report data suggesting no increased risk of childhood brain tumor associated with maternal smoking before or during the pregnancy. Although they report an increased risk associated with father's smoking during the pregnancy, they note that the association disappeared when data supplied by the father, rather than the mother, were considered.

EXCERPTS:

"We report here the results of a population-based case-control study of malignant brain tumours diagnosed between 1985 and 1989 in NSW children with respect to antenatal risk factors, including those *in utero*. The roles of perinatal and postnatal exposure are reported in the companion article in this issue."

"Potential cases comprised all children aged 0 to 14 years, who were newly diagnosed with a primary malignant tumour of the brain or cranial nerves in the period 1985-1989, and reported to the NSW Central Cancer Registry."

"[D]emographic data were sought as well as information about previously postulated risk factors for brain cancer in children (e.g., irradiation, medication), and possible parental exposure to sources of N-nitroso compounds, their precursors or modulators of their metabolism."

"Questions relating to the mother's smoking habits were 'Did you ever smoke at least once a day for 3 months or longer up until the pregnancy with (child)?', 'Did you smoke during your pregnancy with (child)?' and 'Were you regularly exposed to tobacco smoke (a) of (child's) father?, (b) of any other household member? or (c) at work?'."

"No link was seen with the mother's smoking of tobacco either before or during pregnancy. Father's smoking for at least 3 months before the pregnancy was associated with a 2-fold risk of CBT and exposure during pregnancy of women to tobacco smoke of the child's father doubled the risk of CBT (OR = 2.2, 95% CI 1.2 to 3.8; adjusted for smoking habit of mother). However, no increasing risk was seen with increasing use of cigarettes and after stratification by source of information (father or mother), the increased risk was present in the proxy data (ORs of 5.5 and 4.2, respectively, for the 2 smoking variables just mentioned) but not in those obtained directly from the father (ORs of 1.0 and 1.1). No increased risk was found with mother's exposure to tobacco smoke either of other household members (OR = 1.3, 95% CI 0.6 to 2.8) or at work (OR = 0.4, 95% CI 0.4 to 1.4)."

"An association of father's smoking habits with CBT has been claimed by 2 previous case-control studies . . . Although in the present study a 2-fold increased risk was associated with either 'father smoking for at least 3 months at any time before the pregnancy' or 'mother being exposed to father's smoke during pregnancy', no 'dose-response' effect was seen and the excess risk was confined to information obtained from proxies (mothers) giving rise to doubt about the finding. No case-control investigation of brain tumours, including the present study, has yet implicated maternal smoking. . . . If the effect of tobacco seen here is real, the present data cannot distinguish between the effects of: a male factor associated with smoking somehow transferred through sperm; a female factor influenced by passive smoking before or about the time of conception; or subsequent exposure of the child *in utero*."

"[T]he relatively crude analysis in this study, adjusted for mother's body mass index at the start of pregnancy, found rising risks for increasing consumption during pregnancy of cured meats, which have high levels of N-nitroso compounds and their precursors. Moreover, a protective effect was linked with vegetables, many of which high levels of vitamins (A, C or E) in addition to nitrates and/or nitrites."

[2] **McCredie, M., Maisonneuve, P., and Boyle, P., "Perinatal and Early Postnatal Risk Factors for Malignant Brain Tumours in New South Wales Children," *International Journal of Cancer* 56: 11-15, 1994 [Issue 68, Item 31]**

This study reported a statistically significant risk of childhood brain tumor associated with pacifier use. The authors briefly noted that their data suggested no association of brain tumor risk with smoking by a household member.

EXCERPTS:

"We report here the results of a population-based case-control study of brain tumours diagnosed as malignant between 1985 and 1989 in NSW children with respect to perinatal and postnatal risk factors. The roles of antenatal exposures are reported elsewhere."

"Questions related to possible sources of exposure to N-nitroso compounds, their precursors or modulators of their metabolism. Common sources, identified through a literature review, included drinking water, medication, diet, supplementary vitamins, tobacco smoke and the use of a dummy (pacifier); the list was not exhaustive."

"In respect to the N-nitroso hypothesis, no association was found with exposure of the child to tobacco smoke from another member of the household."

"The main finding in this study was the lack of association found with many factors previously demonstrated in one or more studies to be linked with an elevated risk of CBT. Of the *a priori* hypotheses investigated, perhaps the most interesting finding was that of a 2- to 3-fold increased risk of CBT associated with the child's use of a dummy (pacifier). . . . [T]here is insufficient support to claim a causal role and more information will be required from other studies to verify this observation. Nevertheless, experimental data suggest such a possibility. Until recently, dummies and teats for baby's bottles have been made of rubber, which is known to contain N-nitroso compounds, and these have been found to migrate easily into liquid infant formula, orange juice and simulated human saliva."

[3] **Tredaniel, J., Boffetta, P., Saracci, R., and Hirsch, A., "Environmental Tobacco Smoke and the Risk of Cancer in Adults," *European Journal of Cancer* 29A(14): 2058-2068, 1993 [Issue 63, Item 30]**

The authors of this study, three of whom are affiliated with the International Agency for Research on Cancer (IARC), review published epidemiologic studies on ETS exposure and cancers of the lung, urinary bladder, uterine cervix, nasal sinus, breast, brain, colon, endocrine system, and all sites combined. They claim that a relationship between ETS exposure and lung cancer is "definitely established," but that there is "no final evidence" for an association at the other sites. *See also* issue 62 (Item 41) of this Report, December 17, 1993.

EXCERPTS:

"This paper will review the epidemiological evidence between ETS exposure and cancer in adults, with special emphasis on cancers in organs other than the lungs."

"It is very unlikely that chance alone might explain the association between ETS and lung cancer: even if the increase in risk is not likely to be higher than 40%, the size of the populations which have been studied is large enough to exclude with reasonable confidence the possibility that it originated only by random statistical variation; overall, 3453 lifelong non-smoking lung cancer cases have been included in the published studies, 2716 of them (79%) after the 1986 reports which already concluded on the carcinogenic role of ETS. On the other hand, considering that the association between ETS exposure and cancers in adults other than lung cancer, if existing, is presumably weak, one must wonder whether chance alone could explain the reported findings. In addition, most of the studies which we have reviewed, especially the initial ones, although sometimes suggestive of a positive effect, have had several deficiencies which can substantially bias study results, increasing the difficulty in their interpretation, especially if the likely effect of ETS is small. Finally, unrecognised confounding factors may have produced spuriously positive results."

"The criteria to consider, in judging whether an association observed between a particular factor and disease is one of cause and effect, have been extensively discussed. All the available data seem to fulfill, at the present time, and at least to reasonable degree, the criteria needed to accept a causal link between ETS and lung cancer among lifelong non-smokers."

"The problem is much more complicated when dealing with ETS and cancers other than the lung. A dose-response relationship has not been considered in the majority of the studies. Few studies attempted to characterize exposure more specifically than using the numbers of smokers at home."

"Biological plausibility must especially be questioned."

"In particular, the results of elevated risk of sinonasal cancer -- in addition to the risk of lung cancer -- strengthen the plausibility of carcinogenic hazards of sidestream smoke inhalation through the nose."

"When found, the association between ETS exposure and cancers not related to active smoking is difficult to interpret, and necessarily regarded with caution. We may be seeing the effect of unrecognised confounder(s). On the other hand, other possible mechanisms may be involved."

"The ubiquitous presence of tobacco smoke in homes, workplaces, public and private areas has made, until recently, exposure to ETS virtually unavoidable. Involuntary exposure to tobacco smoke has only been intensively investigated as a risk factor for disease in non-smokers in the past decade. Consequently, the evidence on ETS is more limited in scope than for active smoking, and controversy remains concerning the association of ETS with certain diseases. Although ETS-related lung carcinogenesis can be considered as definitely established, there is, as yet, no final evidence of an association between ETS exposure and cancer at sites other than the lung. However, such a conclusion is still based on limited information, and considering the large number of studies which have resulted in widely divergent findings, methodologically improved studies with larger sample sizes are needed. There are sites such as the nasal cavity and the sinuses for which the available evidence strongly suggests the presence of an effect, while for other sites, such as the urinary bladder, it rather suggests the absence of an association. The suggestion of an effect on other sites, such as the uterine cervix, the brain and the breast is more difficult to interpret. Yet, full resolution would seem unnecessary for the evolution of public policy on ETS, an air pollutant with a readily controllable source. Our priority must be to continually encourage the reduction in tobacco use."

[4] Zheng, W., McLaughlin, J.K., Chow, W.-H., Chen, H.T.C., and Blot, W.J., "Risk Factors for Cancers of the Nasal Cavity and Paranasal Sinuses Among White Men in the United States," *American Journal of Epidemiology* 138: 965-972, 1993 [Issue 68, Item 32]

The authors of this study, which was based on data collected from the next-of-kin of deceased men who had nasal cancer, report that their data suggest an increased risk of nasal cancer among men whose spouses smoked. The reported risk for spousal smoking is marginally statistically significant, and is larger than the risk reported for men who were themselves heavy smokers.

EXCERPTS:

"To recruit a large number of cases for a case-control study of cancer of the nasal cavity and sinuses, we identified all deaths attributed to this cancer in the United States in 1985, as an adjunct to a 1986 national survey. Here, we report the results from this study."

"The study was based on data collected as part of the 1986 National Mortality Followback Survey conducted by the National Center for Health Statistics (NCHS). . . . A structured questionnaire was sent to next of kin of these selected decedents to obtain information on the decedent's demographic characteristics, history of tobacco use, usual intake of alcoholic beverages, usual occupation and duration in that job, dietary patterns, and other factors."

"A total of 168 deaths from nasal cancer among white men aged 45 and over were included in the study."

"A 20 percent excess risk of nasal cancer was associated with ever having smoked cigarettes. . . . [A]mong nonsmokers, cases more often than controls had a spouse who smoked cigarettes (OR = 3.0, 95 percent CI 1.0-8.9), after adjustment for age and alcohol use. The association appeared stronger when the maxillary sinus cancers were evaluated (OR = 4.8, 95 percent CI 0.9-24.7). Although there was no evidence of an increased risk with number of cigarettes smoked by the spouse overall, when restricted to maxillary sinus cancers, there was some suggestion of increasing risk by amount smoked."

"Our study has provided further evidence that environmental factors play an important role in the etiology of nasal cancer. . . . A significant excess risk was observed among nonsmokers whose spouse smoked, which lends support to earlier observations in Japan that passive smoking may also increase risk of nasal cancer. The odds ratio associated with spousal smoking (OR = 3) was actually higher than the odds ratio for heavy smoking (OR = 2), but the confidence limits about the former were wide (due to the relatively small numbers of nonsmoking men married to smokers). We also found a number of occupations (e.g., woodworkers and textile workers) associated with elevated risks of nasal cancer."

"Alcohol consumption . . . was also linked to a significantly elevated risk of nasal cancer."

"Our dietary analyses revealed a suggestive protective effect of vegetable consumption, indicative of a possible role for dietary factors in the development of nasal cancer."

"High consumption of salted/smoked foods was linked to an increased risk of nasal cancer in this study."

"The limitations of this study should be considered when interpreting the results. All information was obtained from

next of kin, which raises concerns about the accuracy of exposure history of the study participants."

"In summary, this nationwide case-control study confirmed earlier reports that cigarette smoking, passive smoking, and certain occupational factors may increase risk of nasal cancer."

Other Health Issues

[1] **Arnold, C., Makintube, S., and Istre, G.R., "Day Care Attendance and Other Risk Factors for Invasive *Haemophilus influenzae* Type b Disease," *American Journal of Epidemiology* 138(5): 333-340, 1993 [Issue 63, Item 31]**

Haemophilus influenzae type b (Hib) is a bacterium associated with several disease outcomes, including meningitis, particularly in young children. Based on a study of children in Oklahoma, the authors report that day care attendance was statistically significantly associated with an increased risk of meningitis due to Hib infection. Smoking in the home was investigated as a potential risk factor; no statistically significant increase in risk was reported.

EXCERPTS:

"The introduction of an effective vaccine makes implementation of a vaccination program against *Haemophilus influenzae* type b (Hib) disease a major public health concern."

"We conducted a population-based matched case-control study of all reported cases of invasive Hib disease occurring in the state of Oklahoma in 1986 and 1987. We examined the role of previously reported risk factors: day care, young siblings in the home, crowding in the home, tobacco smoke pollution, socioeconomic status, race, breast feeding, and Hib polysaccharide vaccine."

"Our primary analysis focused on the risk of Hib disease associated with day care attendance. When cases were considered irrespective of anatomic site, the day care OR for Hib disease found in our study was similar to that found for our highest level of crowding in the home (a ratio of two or more people per bedroom relative to less than 1.5 per bedroom) and having three or more children under 6 years of age in the home. Higher family income was an independent marker of risk: There was a protective effect of an annual income greater than $20,000 relative to an income of less than $10,000 that was similar in magnitude to the increased risk associated with day care attendance."

"Although there were no important or statistically significant differences in risk of the different types of Hib disease associated with the other risk factors, the risk associated with day care attendance was almost entirely for Hib meningitis."

"A clear dose-response effect for exposure to day care and Hib meningitis was demonstrated, with increasing risk associated with both increasing hours of day care per week and increasing numbers of children per room. This supports the hypothesis of a direct relation between day care attendance and Hib meningitis."

"In addition to day care attendance, crowding in the home, number of young children in the home, household income, tobacco smoke pollution, and race were independently associated with risk of Hib disease."

"The protective effect of breast feeding in the subgroup of children under 12 months of age was substantial and was statistically significant."

"Although exposure to Hib polysaccharide vaccine appeared to be protective, the effect did not reach statistical significance."

"[A]fter we controlled for number of young children in the home, crowding, maternal education, and income, there was no independent association of tobacco smoke pollution or race with day care."

[2] **Davis, D.L., Dinse, G.E., and Hoel, D.G., "Decreasing Cardiovascular Disease and Increasing Cancer Among Whites in the United States from 1973 Through 1987: Good News and Bad News," *Journal of the American Medical Association* 271: 431-437, 1994 [Issue 66, Item 25]**

Reporting on a mathematical model for comparing cancer mortality rates or incidence rates over time, the authors suggest that recent increases in cancer may be due to "unrecognized causes" that have been introduced in the past several decades. ETS is not discussed in the paper.

EXCERPTS:

"While cigarette smoking is the single most important known cause of cancer and other chronic diseases today, about 70% of cancer is not generally linked to smoking."

"This article explores past trends in cardiovascular and cancer mortality for age-specific groups of the US white population from 1973 through 1987. Drawing on data developed throughout this time period by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, we also present an extensive analysis of trends in cancer incidence across successive birth cohorts and time periods."

"The mortality rate for a specific cause refers to the proportion of the general population that dies from that cause."

"Cancer incidence measures the rate at which new cancer cases arise among all persons who are at risk."

"[C]ardiovascular mortality dropped between 1973 and 1987 in nearly every age group, whereas cancer mortality dropped in the younger groups but rose in the older groups. For example, in the combined age groups 0 to 54 years and 55 to 84 years, cardiovascular mortality decreased 42% and 33%, respectively. In contrast, during the same 15-year period, cancer mortality decreased 17% in the younger group but increased 12% in the older group."

"[B]etween 1973 and 1987, the rates of all causes of mortality combined decreased 19% from 3335.2 to 2688.9 per 100,000 US whites. During the same period, cardiovascular mortality rates declined 36% from 1894.8 to 1203.8 per 100,000 US whites, whereas cancer mortality rates increased 10% from 756.5 to 834.9 per 100,000 US whites. . . . In 1973, 23% of the deaths among persons in the 65- to 74-year-old group were due to cancer, but by 1987, this proportion had grown to 31%. By 1987, even though proportionally fewer people in this age group died of all causes, relatively more of them died of cancer."

"Incidence rates for all cancers generally increased over time for men and women of all ages, as indicated by comparing the later two time periods with the baseline period 1973 through 1977."

"With respect to smoking-related cancers, incidence rates increased more than 50% during the 15-year interval among women but showed little change among men. In fact, over a wide range of ages, smoking-related cancer among women increased in each successive time period, with the largest increases occurring in the 65- to 74- year-old group. Among men, increases in smoking-related cancer were restricted mainly to the oldest age groups. Although the rate of increase for women was proportionally much larger than for men, the actual incidence of smoking-related cancer was still much larger among men."

"Regarding all cancers other than those related to smoking, the incidence rates did not change much among women during the 15-year interval but rose 19% among men. Thus, men incurred 19% more cancer not linked to smoking than their peers a decade previously. For women, one notable exception was breast cancer incidence, which rose during the period of observation. Rates were 19% higher among those diagnosed in 1983 through 1987 compared with those diagnosed in 1973 through 1977. . . . [T]he increase in breast cancer incidence occurred mainly in women older than 55 years and primarily during the time period 1983 through 1987."

"Men born in the 1940s had nearly a twofold greater risk of contracting cancer compared with those born at the turn of the century in the baseline birth cohort 1888 through 1897."

"Successive birth cohorts of women have experienced dramatic increases in smoking-related cancer, with women born in the 1920s and 1930s developing six times more cancer than women in the baseline birth cohort 1888 through 1897. . . . Among men, the incidence of smoking-related cancer increased with birth cohort to the point where rates for men born in 1923 through 1932 were about 40% greater than for men born in 1888 through 1897."

"The good news about cancer remains the impressive declines in mortality in persons younger than 55 years and in smoking-related risks for men of most ages. The bad news is that, according to the model we have developed here, recent birth cohorts of Americans aged 20 years and older are developing higher rates of all forms of cancer compared with those born just before the turn of the century. The incidence of cancer not related to smoking estimated in recent generations of men and women was 210% and 30% higher, respectively, than it was in persons born in the late 1800s. As for smoking-related cancer, incidence rates for recent generations of women were about five times higher than at the end of the last century, while rates for their male contemporaries have dropped from a peak in the first quarter of this century to about the same levels as occurred almost a century ago."

"[C]ancer-causing hazards in addition to smoking have been introduced into the population in the past several decades. Pinpointing these as yet unrecognized causes of cancer might lead to primary preventive strategies that could yield successes comparable to those recently achieved from smoking reduction in US men."

"[T]he recent increases in cancer cannot stem solely from causes shared with cardiovascular disease, such as smoking and a high-cholesterol diet, but must reflect other environmental factors."

[3] **Fortier, I., Marcoux, S., and Brisson, J., "Passive Smoking During Pregnancy and the Risk of Delivering a Small-for-Gestational-Age Infant," *American Journal of Epidemiology* 139(3): 294-301, 1994 [Issue 67, Item 29]**

This study reports no statistically significant associations between home or workplace ETS exposure and the risk of having an infant with lower than expected birth weight.

EXCERPTS:

"The objective of our analysis was to further assess the relation between maternal passive smoking during pregnancy and the risk of delivering a small-for-gestational-age (SGA) infant. We attempted to overcome some of the limitations of the previous studies in the following ways: our exposure data pertain to passive smoking at home and in the workplace, the associations are described for each surrounding separately, the analysis controls for all known confounders, including selected job characteristics, and the dose-response relation between passive smoking and the risk of SGA is also assessed."

"Among nonsmokers, 49 percent were exposed to environmental tobacco smoke, either at home only (13 percent), at work only (28 percent), or in both surroundings (8 percent). . . Passive smokers included a larger proportion of nulliparae and tended to have higher caffeine intakes than other nonsmokers. Among women who had a paid occupation, passive smokers were more likely to work on evenings or nights and to have jobs involving lifting or long standing periods than unexposed women."

"Overall, nonsmokers passively exposed to tobacco smoke were at little or no higher risk of delivering a SGA infant (OR = 1.09, 95 percent confidence interval (CI) 0.85-1.39) than unexposed women. Passive smoking at home only was not related to SGA (OR = 0.98). . . . [B]eing passively exposed at work only yielded an adjusted odds ratio of 1.18 (95 percent CI 0.90-1.56). The relation between SGA and passive smoking at work only was further examined. The risks of SGA increased slightly but consistently when the weekly hours of exposure, the number of weeks of exposure during pregnancy, and the subjective intensity of exposure increased. However, none of the trends was statistically significant."

"We observed a modest increase in the risk of delivering a SGA infant in pregnant nonsmoking mothers exposed to passive smoking in the workplace. The point estimates increased consistently with the duration and the intensity of exposure, which supports the hypothesis that passive smoking during pregnancy may affect fetal growth. However, our results need to be interpreted with caution because the associations are weak, the confidence intervals all include null values, the tests for trends are not conclusive, and the association is not found in women exposed to smokers at home only."

"[T]he exposure may indeed be more important in the workplace than at home since the number of smokers and the environmental conditions (e.g., ventilation, room size, insulation) may differ in these two surroundings. . . . [A]s the measure used to assess exposure at home (smoking habit of family members) differs from that used to assess exposure at work (hours of exposure), results may not be comparable. . . . [S]moking habit of family members is thought to be a less accurate measure than is the duration of exposure. If so, the associations with passive smoking at home would be more likely to be underestimated due to misclassification."

"Given the difficulty of documenting small effects in epidemiologic studies, in our view, future investigations are not likely to clarify the relation of passive smoking to SGA unless they are restricted to nonsmokers, are based on large prospective cohorts, document exposure in the several possible environments and in different periods of pregnancy, and include a biologic marker of exposure as a supplement to detailed questionnaire data."

[4] **Matarasso, A., "Environmental Tobacco Smoke: The Risks of Passive Smoking in Facial Surgery," *Annals of Plastic Surgery* 31: 573, 1993 [Issue 67, Item 30]**

In this letter to the editor, the author suggests, based on one case study, that ETS exposure could adversely influence the healing process following facial surgery.

EXCERPTS:

"In plastic surgery, the harmful effects of *primary* cigarette smoking . . . following surgery and during wound healing have been well documented. . . . What has not been subject to review are the effects of *passive smoking*. One could extrapolate from what is already known about passive smoking and its effects on patients to speculate on instances of exposure to environmental tobacco smoke (ETS) and to take similar, necessary precautions."

"A couple that had been together for 44 years -- living and working -- recently underwent facial rejuvenation surgery on the same day. The husband's cigarette use consisted of more than 100 packs per year. . . . In the early postoperative period, [the nonsmoking wife] experienced areas of skin ischemia, resulting in superficial epidermolysis and pigmentary changes."

"Environmental tobacco smoke results in involuntary exposure derived from 'mainstream' and 'sidestream' smoke. . . . Although the observations here are anecdotal and wound healing is a multifactorial process, in view of what has been clearly established regarding the adverse effects of primary cigarette smoking, the preponderance of evidence suggests that it is advisable to consider ETS as a possible deleterious factor. When screening patients and operating, the effect of ETS on delayed wound healing or tissue necrosis may in fact be an additional risk factor that can confound procedures that necessitate mobilization of flaps, and should not be underestimated."

[5] **Olds, D.L., Henderson, C.R., and Tatelbaum, R., "Intellectual Impairment in Children of Women Who Smoke Cigarettes During Pregnancy," *Pediatrics* 93: 221-227, 1994 [Issue 67, Item 31]**

Although this paper focuses on maternal *active* smoking during pregnancy, the authors report that smoking by the mother approximately four years after the child's birth was associated with a three-point difference (not statistically significant, however) in the IQ scores of children of smoking mothers compared to children of nonsmokers.

EXCERPTS:

"In the current paper we examine whether the relationship between maternal prenatal cigarette smoking and children's intellectual impairment during the first 4 years of life remains after controlling for a wide range of potentially confounding influences."

"Interviews with the mother were conducted at registration during pregnancy, at the 34th week of gestation, and at 6, 10, 22, 34, and 46 months of the child's life."

"When smoking was defined by level of postnatal (46-month) smoking, the adjusted difference in children's IQs (averaged across 3 and 4 years of age) between those whose mothers smoked 0 and those whose mothers smoked 10+ cigarettes per day was 3.09 points (95% CI: -0.93, 7.11). . . . [T]he greatest difference in children's intellectual functioning was found for cigarette smoking measured at the end of pregnancy."

"Children born to women who smoked heavily during pregnancy (10+ cigarettes per day), and who did not receive nurse-visitation services, had IQ scores at 1 and 2 years of age that were nearly 7 points lower, and at 36 and 48 months that were 9 points lower than children born to women who did not smoke during pregnancy. These differences were explained in part by associated differences in social class, maternal education, IQ, qualities of caregiving, and conditions in the home environment. Even after control for these biasing influences, however, a significant difference of 4.35 IQ points remained at 3 and 4 years between the children of women who smoked substantially versus those who did not smoke at all during pregnancy. This four-point effect, although small, is comparable with the adverse influence of low levels of lead exposure on preschoolers' IQ test performance where the children do not show symptoms of lead encephalopathy."

"[W]e did not assess fully the child's exposure to side-stream smoke during the first 4 years after delivery. It is revealing, nevertheless, that maternal post partum smoking was less predictive of the children's intellectual development than was prenatal smoking. We assume that a substantial portion of the children's exposure to passive smoke is likely to come from the mother, and that where the mother smokes other individuals in the household also are likely to smoke. Clearly, more work needs to be performed on this topic, using more valid and reliable measures of passive smoking."

"Moreover, it is clear that women who smoked 10+ cigarettes per day were substantially different from those who did not smoke at all. It is possible that we did not measure all possible confounders and that some other unidentified variable accounts for the differences in children's IQs associated with maternal prenatal smoking levels."

[6] **Owen, M.J., Baldwin, C.D., Swank, P.R., Pannu, A.K., Johnson, D.L., and Howie, V.M., "Relation of Infant Feeding Practices, Cigarette Smoke Exposure, and Group Child Care to the Onset and Duration of Otitis Media with Effusion in the First Two Years of Life," *Journal of Pediatrics* 123: 702-711, 1993 [Issue 65, Item 32]**

Based on data collected from a sample of almost 700 infants in Texas, the authors report that supine feeding position and early initiation of group child care were associated with an earlier onset of otitis media with effusion (OME). They also report that an increase in the time with OME was associated with shorter duration of breast-feeding, more packs of cigarettes smoked in the home, and increased hours per week spent in child care.

EXCERPTS:

"The relation of infant feeding practices, cigarette smoke exposure, and group child care to the onset and duration of otitis media with effusion (OME) was evaluated in a cohort of 698 healthy infants prospectively monitored by tympanometry in the home every 2 to 4 weeks until 2 years of age. Except for an experimental group of children who were offered early tube placement, the study children received conventional care from their personal physician

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or clinic. We used LISREL, a structural equation modeling procedure (computer software), to explore associations between environmental variables and OME onset and duration while controlling for interrelations among the variables."

"[N]o significant differences were found between the sample at the start of the study and those still active at 2 years of age for distribution of subjects by sex, ethnicity, frequency of breast-feeding, and frequency of smoker(s) in the home."

"Forty-one percent of the subjects were exposed to cigarette smoke in their home. Thirty-one percent of the fathers smoked, 20% of the mothers smoked, and 12% of subjects had other smokers in the home."

"In our sample, OME was common and its onset was early."

"[E]arly age at onset of OME predicted more OME during the first year of life . . . In addition, more OME in each age period studied was associated with more OME during the next 6 to 12 months."

"The apparent increased amount of OME seen in subjects who were breast fed for a short period, in comparison with those who were never breast fed, is likely to be explained by the finding that mothers of high SES, who were more likely to breast-feed, were also more likely to expose their children to group child care at earlier ages. This possible explanation emphasizes the importance of the use of statistical methods to control for interactions among the variables."

"Although it was not a common practice in our study sample, supine feeding position was related to earlier age at onset of OME."

"We found a significant association between the number of cigarettes smoked by household members and the amount of OME in the second year of life. The timing of this effect on the second year of life, but not the first, may suggest that parents are less protective of older children and are more likely to smoke around them. alternatively, the mechanism of this effect may require time to develop (e.g., allergy) or may be cumulative."

"Many of the previous studies examined the smoking practices of each parent separately. In a preliminary exploration of our data with univariate analysis, we found no significant association between OME duration and whether each parent smoked or how much each parent smoked individually. This finding and the dose-response shape of the effect, plus the selective impact of smoking on OME diagnosed during the second year of life, all suggest that postnatal effects of smoke exposure are important. We did not collect data on maternal prenatal smoking."

"We found that earlier initiation of group child care was associated with earlier onset of OME. The association of a later initiation of group care with more OME during the second year of life probably reflects the finding that more OME occurs at the time that group care starts. The amount of time spent in group care was associated with the amount of OME, particularly in those in group care more than 20 hours per week. We also found that earlier initiation of group care and more time spent in group care were associated with an increased likelihood of having tympanostomy tubes placed in the first year of life."

"The pathogenesis of OME in young children involves a complex interplay between eustachian tube dysfunction and the presence of infection and inflammation of the middle ear. Thus any factor that influences the anatomic structure and physiologic ventilation of the middle ear, the child's exposure to upper respiratory tract infection, or the child's immunologic response can influence the frequency and duration of OME."

[7] **Scragg, R., Mitchell, E.A., Taylor, B.J., Stewart, A.W., Ford, R.P.K., Thompson, J.M.D., Allen, E.M., and Becroft, D.M.O., on behalf of the New Zealand Cot Death Study Group, "Bed Sharing, Smoking, and Alcohol in the Sudden Infant Death Syndrome," *British Medical Journal* 307: 1312-1318, 1993 [Issue 63, Item 32]**

In another paper from the New Zealand study on sudden infant death syndrome (SIDS), the authors report a statistically significant risk of SIDS for infants whose mothers smoked and who shared beds with the infant. The authors suggest that "passive smoking" is the important factor in the claimed association, and suggest that the mother exhales smoke constituents that are breathed in by the infant.

EXCERPTS:

"We report the first systematic analysis of bed sharing as a risk factor for the sudden infant death syndrome using data collected in a population based case-control study which covered a region with 78% of births in New Zealand. We examined how the risk of sudden infant death from bed sharing is related to other factors, particularly maternal smoking. We tested previous hypotheses -- such as hyperthermia, recent infant illness, and overlaying -- put forward to explain the possible association between bed sharing and sudden infant death. In particular, we examined whether maternal alcohol consumption,

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implicated in overlaying, is a risk factor by itself or whether it is confounded by other factors such as maternal smoking."

"Our results do not support the idea that infant bed sharing protects against the sudden infant death syndrome. Instead, they show that infant bed sharing is a risk factor for this syndrome, particularly among infants of mothers who smoke. For these infants, the risk of sudden death increased with increasing duration of bed sharing, although it did not vary with the number of cigarettes smoked by the mother."

"In contrast, we found that neither maternal alcohol consumption nor the thermal resistance of the infant's clothing and bedding interacted with bed sharing to increase the risk of sudden infant death; neither was alcohol a risk factor by itself."

"These results have implications as to the likely mechanism(s) by which bed sharing increases the risk of sudden infant death. They do not support a role for overlaying or hyperthermia, for the following reasons. Firstly, if either of these mechanisms was involved the increase in risk of sudden death from bed sharing should have been similar for all infants, regardless of whether the mother smoked. It seems unlikely that maternal smoking would interact with either of these mechanisms to cause an increased risk due to bed sharing only in infants with mothers who smoke."

"Unless there is a third unknown common factor, the interaction between maternal smoking and bed sharing suggests these are components of a sufficient cause that involves a passive smoking mechanisms. Some mothers may be smoking in bed with their infants, although this may not occur commonly because of increasing parental concern in recent years about the effects of passive smoking on children. If few mothers are smoking in bed with their infants, then an alternative explanation for our findings is that rebreathing of expired air from the mother by the infant could lead to hypoxia, as has been postulated to occur in infants dying suddenly who might rebreath [sic] their own expired air when placed prone. . . . Rebreathing may occur, to varying degrees, in all infants who share beds but be most hazardous for infants of smoking mothers."

"Unabsorbed tobacco components from the mother may flow continuously over, and be inhaled by, the baby during sleep, ultimately causing hypoxia and increasing the risk of sudden death. A cumulative exposure by this mechanism would be consistent with the finding of an increased relative risk for infants who usually shared beds in the last two weeks but not in the last sleep."

"If bed sharing is a marker for passive smoking among infants of smoking mothers then our results are consistent with previous epidemiological studies which show that maternal smoking is a risk factor for sudden infant death."

"The observation that paternal smoking did not modify the relative risk from bed sharing was also unexpected. Perhaps infants are placed on the outside of the bed next to the mother, but away from the father, thus limiting their paternal smoking exposure. . . . Further studies of parental smoking and bed sharing may help to explain why we have observed no effect with fathers and no dose response effect with mothers."

"The attributable risk for cases exposed to both risk factors calculated from our data for bed sharing in the last two weeks suggests that about 20% of all sudden infant deaths in New Zealand can be explained by the joint effect of these two factors. . . . Given the difficulty that many people have in stopping smoking, recommendations that parents who smoke should not share beds with their infants may be more effective in lowering the rate of sudden infant deaths than advising them to stop smoking."

ETS Exposure and Monitoring

[1] Brenner, H., and Mielck, A., "Children's Exposure to Parental Smoking in West Germany," *International Journal of Epidemiology* 22(5): 818-823, 1993 [Issue 64, Item 41]

The authors of this study report on the prevalence of maternal and paternal smoking in a sample of households surveyed in West Germany. Estimates of prevalence presented in the paper include, for paternal smoking, 33.7 percent for children less than two years of age, 43.1 percent for those ages two to five, and 46.8 percent for children ages six to 13. Estimates of the prevalence of maternal smoking ranged from 18.9 percent to more than 30 percent.

Excerpts:

"In this paper, we develop and employ an indirect method for deriving estimates of the prevalence of children's exposure to parental smoking from information on active smoking habits, and family and living conditions of adults in the Federal Republic of Germany (FRG)."

"Among children aged 6-13 living in the same household as their father, almost 50% were exposed to paternal smoking. This proportion decreased to 43.1% and 33.7%

among 2-5 year old and 0-1 year old children. . . . There was a striking variation of exposure to paternal smoking by level of school education of the father; paternal smoking prevalence varied between 73.8% for the 6-13 year olds whose father had ≤9 years school education and 23.5% for children of the same age group with better-educated fathers."

"Overall, the prevalence of maternal smoking was considerably lower than the prevalence of paternal smoking, although almost one-third of the children aged 2-13 were exposed to maternal smoking. Again, there were striking differences by level of maternal school education: prevalence of exposure to maternal smoking was almost twice as high among 6-13 year old children of less-educated women (39.7%) compared to children of better-educated women (20.6%)."

"About 60% of the 0-1 year old children and more than two-thirds of the 6-13 year old children were exposed to at least one smoking household member, and about one-third of the children in each of the three age groups was exposed to at least two smoking household members."

"A limitation of our approach is that the quantification of parental smoking is based on self-reported active smoking habits of the parents rather than precise measures of children's inhalation of sidestream tobacco smoked (e.g. by biological markers). . . . As underreporting of active smoking is more likely than overreporting in health surveys, the true prevalence of parental smoking and average numbers of cigarettes smoked per day by smoking parents are likely to be even higher than estimated in this study."

"Another limitation is the potential for selection bias as reflected in the overall response rate of only about 66%."

"Maternal smoking prevalence was somewhat lower for children aged 0-1 than for older children. Although this may reflect high quit rates during pregnancy followed by high relapse rates in the years following childbirth, the fact that a similar pattern was observed for paternal smoking supports the possibility of the beginning of a secular trend towards lower parental smoking rates. A definite answer to this question is not yet possible with currently available data."

"[T]he high prevalence of exposure to parental smoking in Germany implies that a large proportion of respiratory diseases among children, including such severe conditions as childhood asthma, is likely to be due to parental smoking and should therefore be preventable by reducing smoking among parents. It should be noted that the associations reported in epidemiological studies could substantially underestimate the true associations due to inaccuracies in reporting smoking habits, particularly as one might suspect underreporting of smoking in parents with symptomatic children in many studies."

[2] Cook, D.G., Whincup, P.H., Jarvis, M.J., Strachan, D.P., Papacosta, O., and Bryant, A., "Passive Exposure to Tobacco Smoke in Children Aged 5-7 Years: Individual, Family, and Community Factors," *British Medical Journal* 308: 384-389, 1994 [Issue 67, Item 32]

Using data on parental smoking and saliva cotinine measurements collected from English and Welsh children, the authors report that maternal smoking was most related to cotinine level, even though fathers reported smoking more cigarettes. The authors also reported a statistical correlation between cotinine levels in children not exposed at home and the prevalence of smoking in the community.

EXCERPTS:

"We present an analysis of the relation between cotinine concentration and questionnaire data in children aged 5-7 from 10 towns in England and Wales. We examine the importance of parental exposure as opposed to other sources; exposure among children from non-smoking households; and the social and geographical pattern of passive exposure to tobacco smoke in children."

"The study was carried out in 10 towns in England and Wales -- five with high adult cardiovascular mortality and five with low mortality."

"Fifty three percent (1610/4030) of children were exposed to at least one smoker."

"Geometric mean cotinine concentration varied greatly with source of exposure from 0.29 ng/ml in children with no identified source of exposure to 4.05 ng/ml when both parents smoked, a 13.7 fold increase. In the 20 children in whom both parents smoked more than 20 cigarettes a day the geometric mean cotinine was 9.03 ng/ml (95% confidence interval 6.73 to 12.1)."

"Our data confirm that parental smoking is the most important source of passive exposure to smoke in young children and show a clear dose response with number of cigarettes smoked a day. While mothers were less likely to smoke than fathers, the effect on cotinine concentrations when they did so was greater, presumably because they spend more time with the children. The difference in effect was small at low levels of smoking, but pronounced at higher levels. One interpretation is that fathers who smoke heavily are less likely to do so in the presence of

the child than mothers who smoke heavily. Overall, maternal smoking contributed more to the children's burden of cotinine than did paternal smoking. Other people smoking in the household and being looked after by someone from outside the household who smoked also made small contributions to exposure. However, such sources of exposure were relatively uncommon and when present were less important than parental smoking."

"[N]icotine is not entirely specific to tobacco. It is also found in small amounts in peppers, aubergines, and potato skins. We have previously argued that these are unlikely to greatly influence cotinine concentration. The uniformly low concentrations among our non-exposed children suggest that either the higher concentrations seen in the exposed children are due to smoking or the dietary factors are almost entirely confounded with smoke exposure in the home, which seems implausible. Even among our non-exposed children the concentrations of cotinine correlate with community smoking habits, which suggests that any other sources of cotinine make only a very small contribution."

"The social class and geographical differences in cotinine concentrations emphasize the variation in passive exposure to tobacco smoke among children from different backgrounds."

"Though the identified sources of exposure were the most important determinants of variation in cotinine concentrations, other sources and modifying factors clearly existed. Eighty eight percent of children not exposed at home and not looked after by a smoker had cotinine detected in their saliva. Cotinine concentration in non-exposed children was related to both social class and town of residence and was presumably attributable to sources we did not inquire about. This is supported by the finding that the cotinine concentrations in non-exposed children were directly related to the community level of smoking."

"7-11% of the population burden of cotinine was in children not exposed to any of the sources we asked about. The correlation between cotinine concentrations in such children and the prevalence of smoking in the community suggests that passive smoking should be viewed as a community exposure rather than simply as an aspect of family lifestyle."

[3] **Crawford, F.G., Jeffrey, A., Santella, R.M., Mayer, J., and Perera, F.P., "Biomarkers of Passive Smoking in Children and Their Mothers," *Proceedings of the American Association for Cancer Research* 34: 263, 1993 [Issue 65, Item 33]**

The authors of this abstract claim that, in a survey of biological markers for carcinogenesis in New York City preschool children and their mothers, ETS exposure is reportedly correlated with levels of cotinine, hemoglobin adducts, and albumin adducts.

EXCERPTS:

"We are investigating biologic markers of carcinogenesis and environmental tobacco smoke (ETS) in New York City preschool children and their mothers. There are 3 exposure groups: (a) mother smokes, (b) another household member smokes, (c) no smoker in the home. Among mothers, a significant association was seen between smoking groups and mean levels of cotinine, 4-aminobiphenyl-hemoglobin (4-ABP-Hb), and polycyclic aromatic hydrocarbon(PAH)-albumin adducts. In children, ETS was significantly associated with cotinine, and approached significance with 4-ABP-Hb. PAH-albumin adducts were correlated with amount of maternal smoking. The study demonstrates significant effects of ETS exposure on levels of cotinine, 4-ABP-Hb, and PAH-albumin adducts and points to potential risks for young children."

[4] **Eliopoulos, C., Klein, J., Phan, M.K., Knie, B., Greenwald, M., Chitayat, D., and Koren, G., "Hair Concentrations of Nicotine and Cotinine in Women and Their Newborn Infants," *Journal of the American Medical Association* 271(8): 621-623, 1994 [Issue 67, Item 33]**

The authors of this study report that measurements of nicotine and cotinine in the hair of "passive smoking" mothers and their infants were intermediate between measurements from active smoking women and non-smoking women. This study expands on data reported previously in a preliminary report. *See* issues 53 and 55 of this Report, August 6 and September 10, 1993.

EXCERPTS:

"In the present study we describe the distribution characteristics of nicotine and its major metabolite, cotinine, in maternal and neonatal hair. These data suggest that accumulation of nicotine and cotinine in neonatal hair may be used clinically and in laboratory studies to estimate fetal exposure to maternal cigarette smoking."

"Mothers who were active smokers, passive smokers, or nonsmokers were identified in two newborn nurseries in Toronto, Ontario, 1 to 3 days after delivery. . . . Passive smoking was defined as regular and steady gestational exposure to other persons' cigarette smoke, either at home (eg, smoking by husband or partner) or in the workplace. Hair samples were obtained by cutting five to seven hair shafts."

"Thirty-five nonsmoking mothers participated in the study. Their mean hair concentrations of nicotine and cotinine were significantly lower than in smoking mothers. Similarly, neonatal hair concentrations of nicotine and cotinine were significantly lower in infants of nonsmokers than in infants of smokers."

"Twenty-three passive smoking mothers and their infants participated in the study. Their concentrations of nicotine and cotinine were intermediate and significantly different from those of both the smokers and nonsmokers."

"[O]ur results suggest that maternal and fetal hair may better estimate long-term systemic exposure to the toxic constituents of cigarettes than the reported consumed dose and thus may yield a better prediction of fetal/neonatal risk."

"During the last few years there has been increasing awareness of the serious health risks inflicted by passive exposure to cigarette smoke. In a recent study, Makin et al. documented impaired neurodevelopment in infants exposed in utero to passive maternal smoking compared with nonsmoking controls. Analysis of such data is complicated because of the potential confounding variables in assessing toddler achievements in cognitive tests; however, these researchers controlled for known confounders in their model. On the other hand, the degree of fetal exposure to cigarette smoke could not be evaluated in the absence of a biological marker. Our data indicate that, indeed, passive smoking pregnant women and their infants accumulate nicotine and cotinine to measurable levels. These data confirm our preliminary findings in four passive smokers who were initially included in a group of nonsmokers. Because hair accumulation of cotinine reflects long-term exposure, it may provide a more accurate determination of fetal exposure to cigarette smoke than the reported number of cigarettes consumed."

[5] Holz, O., Meissner, R., Einhaus, M., Koops, F., Warncke, K., Scherer, G., Adlkofer, F., Baumgartner, E., and Rudiger, H.W., "Detection of DNA Single-Strand Breaks in Lymphocytes of Smokers," ***International Archives of Occupational and Environmental Health*** **65: 83-88, 1993 [Issue 65, Item 34]**

Based on an analysis of DNA from blood cells of five smokers, five nonsmokers experimentally exposed to ETS, and five "nonexposed" nonsmokers, the authors claim to find an increase in DNA single-strand breaks (a possible parameter of genetic toxicity) in smokers, but not in nonsmokers exposed to ETS.

EXCERPTS:

"DNA single-strand breaks (SSBs) are considered to be an important parameter of genotoxic stress."

"[W]e performed a controlled study using ten male volunteers (five smokers and five nonsmokers) subjected to different smoking conditions and five nonsmoking controls. SSBs were determined at different times after blood sampling and after transportation and were related to DNA repair as unscheduled DNA synthesis (UDS)."

"Tobacco smoke exposure led to an increase in carboxyhemoglobin (COHb) and plasma cotinine levels. . . . SSBs could be detected in all probands with some interindividual day-to-day and morning-to-evening variations. Four of five smokers had an increase in SSBs after smoking. No exposure-related variation in SSB levels could be detected in passive smokers."

"Active smoking caused an increase in SSBs in peripheral blood lymphocytes. This effect could not be found in passive smokers and is consistent with the finding of significantly lower cotinine plasma levels and COHb."

"The variation in the SSB levels in lymphocytes of passive smokers and controls could not be correlated to a particular exposure. Individual levels of SSBs and day-to-day levels varied markedly for unknown reasons."

"Samples that were transported at 0°C to a second laboratory prior to testing showed identical results for some probands but rather different results for others, thus concealing the smoking-related effects."

"The repair of these . . . lesions did not show a smoking-related increase or inhibition, suggesting that the increase in SSBs after smoking is caused by a direct genotoxic effect of tobacco smoke rather than by smoking-related inhibition of DNA repair."

[6] **Nazaroff, W.W., Hung, W.-Y., Sasse, A.G.B.M., and Gadgil, A.J., "Predicting Regional Lung Deposition of Environmental Tobacco Smoke Particles," *Aerosol Science and Technology* 19: 243-254, 1993 [Issue 64, Item 42]**

This paper reports on a methodology that incorporates several models in an attempt to predict respiratory tract particle deposition of ETS. The methodology uses particle size distributions, aerosol dynamics, and a lung deposition model to generate its conclusions.

EXCERPTS:

"To improve our understanding of the risk of ETS exposure, it is important to know the size distributions of ETS particles that deposit in different regions of the respiratory tract. This paper presents a method for predicting regional deposition of ETS particles in human lungs. The method combines experimental data on ETS particle emission profiles with two existing mathematical models: an indoor aerosol dynamics model and a lung deposition model. The paper describes the method and illustrates its application by predicting lung deposition of ETS particles for a selection of residential exposure conditions. The method should be useful in two applications: assessing risk of ETS exposure under varying conditions; and evaluating the effectiveness of control measures."

"Interpretation of particle size distribution measurements after cigarette combustion by a smoking machine in a test room yields an effective emissions profile. An aerosol dynamics model is used to predict indoor particle concentrations resulting from a specified combination of smoking frequency and building factors. By utilizing a lung deposition model, the rate of ETS mass accumulation in human lungs is then determined as a function of particle size and lung airway generation. Considering emissions of sidestream smoke only, residential exposures of nonsmokers to ETS are predicted to cause rates of total respiratory tract particle deposition in the range of 0.4-0.7 ug/day per kg of body weight for light smoking in a well-ventilated residence and 8-13 ug/day per kg for moderately heavy smoking in a poorly ventilated residence. Emissions of sidestream plus mainstream smoke lead to predicted deposition rates about a factor of 4 higher."

"The method proposed here comprises two major stages. In the first stage, an indoor aerosol dynamics model is used to predict the indoor airborne particle size distribution as a function of time. The key input data are as follows: the particle emissions profile from a cigarette; the temporal pattern of smoking; the volume of the building; the ventilation rate; and, if an air filter is active, the filtration rate and efficiency. In the second stage, a lung deposition model is used to relate the airborne particle size distribution to particle mass accumulation in an exposed individual. Key input data for this stage are the age, gender, and activity level of the exposed individual; these parameters determine the lung morphometry, breathing frequency, and tidal volume. The central output of the model is a prediction, for each generation of the respiratory tract, of the mass of environmental tobacco smoke particles deposited over a specified time interval, segmented according to particle size."

"As presently formulated, the model components do not account for processes of evaporation and condensation which, in principle, may occur either in indoor air or within the respiratory tract."

"Our research group is presently applying this method to other environmental tobacco smoke exposure scenarios. We are giving particular attention to the potential for reducing exposure by local ventilation or by the use of portable air cleaners."

[7] **Tribble, D.L., Giuliano, L.J., and Fortmann, S.P., "Reduced Plasma Ascorbic Acid Concentrations in Nonsmokers Regularly Exposed to Environmental Tobacco Smoke," *American Journal of Clinical Nutrition* 58: 886-890, 1993 [Issue 67, Item 34]**

The authors claim to present data supporting lower levels of plasma ascorbic acid, a claimed antioxidant and "anticarcinogen," in persons exposed to ETS. A similar result had been reported previously for smokers.

EXCERPTS:

"Radical-mediated oxidative processes have been implicated in the pathogenesis of chronic and degenerative diseases including cancer and atherosclerotic heart disease. . . . Smokers exhibit reduced concentrations of the antioxidant vitamin ascorbic acid (AA)."

"Environmental tobacco smoke (ETS) is now recognized to predispose exposed individuals to the development of chronic diseases, although little is known about the nature and magnitude of the pathophysiological effects of ETS exposure, or the degree to which these may contribute to increased disease risk. Sidestream smoke contains a greater oxidant load than mainstream smoke and high ambient concentrations of oxidants are likely to be present in inadequately ventilated homes, workplaces, and other enclosed settings where smoking is permitted. We hypothesized that nonsmokers regularly exposed to such conditions were chronically

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oxidatively stressed and thus would exhibit aberrations in AA nutriture similar to smokers. To examine this possibility we compared plasma AA concentrations and vitamin C intakes in a cross-sectional sample of women classified as either active heavy smokers (AS), regular passive smokers (PS), or nonexposed nonsmokers (NNS)."

"Our results confirm previous reports of reduced plasma AA concentrations in AS and additionally show that PS exhibit reduced concentrations relative to NNS."

"In contrast to observations of decreased vitamin C consumption in smokers, we did not observe decreased vitamin C intakes in smoke-exposed populations relative to NNS."

"Reduced plasma AA concentrations were apparent even in AS reporting dietary vitamin C intakes exceeding current recommended dietary allowances (RDAs) for smokers. These data support previous contentions that dispute the recent increase to 100 mg vitamin C/d, the RDA is still inadequate for smokers. . . . Our results additionally suggest that current vitamin C intake recommendations are inadequate to meet the increased needs of nonsmokers regularly exposed to ETS. Plasma AA concentrations were reduced in PS reporting vitamin C intakes up to 250 mg/d, but not at higher intakes."

"In summary, we observed reduced plasma AA concentrations in AS and PS relative to NNS that were not attributable to differences in vitamin C intakes among these populations. These results suggest that, like AS, PS are subjected to severe oxidant exposure. Oxidative mechanisms have been implicated in numerous chronic and degenerative diseases and thus may be involved in the increased risk associated with ETS exposure. Although reductions in plasma AA concentrations in PS may be overcome at higher vitamin C intakes, this is unlikely to completely ameliorate the pathogenic consequences of the underlying oxidant pressure."

Indoor Air Quality

[1] **Anderson, R.C., "Toxic Emissions from Carpets." In: *Building Design, Technology, and Occupant Well-Being in Temperate Climates.* E. Sterling, C. Bieva, and C. Collett (eds.). Atlanta, ASHRAE, 259-264, 1993 [Issue 66, Item 26]**

Rosalind Anderson, president of Anderson Laboratories, describes in this paper her organization's controversial reports of neurological effects and death in mice experimentally exposed to fumes from heated carpet samples. She claims that the results of these tests indicate that irritant and neurotoxic chemicals are present in carpets.

Excerpts:

"For a number of years, there has been concern that some individuals suffer adverse health effects from exposure to chemical emissions of carpeting."

"The American Society for Testing and Materials (ASTM) has published a standardized method, ASTM E [981], for measuring the biological effects of irritant chemicals. In this bioassay, mice breathe a sample of treated air; if irritant chemicals are present, there is a characteristic change in the respiratory rate and pattern (described as sensory or pulmonary irritation)."

"Using ASTM E 981 for studies of the emissions from offgassing carpets, we have found sensory and pulmonary irritation and observed striking neuromuscular effects. We believe this is an important demonstration of adverse health effects of carpet emissions."

"Approximately 3 ft^2 of each carpet was placed in a . . . chamber . . . and warmed by an external heating blanket to an air temperature of 37°C for one hour prior to the experiment. The carpet was left in the sample chamber between tests and reheated before each test."

"For each test four mice were positioned in a glass exposure chamber. The head of each mouse extended into the exposure area . . . while the body was within a glass side arm."

"Emissions from some complaint carpets caused sensory irritation."

"Sensory irritation varied but generally increased with repeat exposures of the mice to complaint carpet emissions."

"Most complaint carpets caused marked pulmonary irritation on all exposures. . . . The tracing of the respiratory excursions of this mouse shows the characteristic pause before inspiration that defines pulmonary irritation."

"Generally pulmonary irritation was greater after multiple exposures of the animals to the complaint carpet emissions."

"Following exposure to emissions released by complaint carpets, animals demonstrated altered posture, hypoactivity or hyperactivity, paralysis of one or more limbs, and/or death. . . . Very few clinical changes were seen after the first exposure; progressively more changes

were seen after the second, third, and fourth exposures during the two-day period."

"These results demonstrate that certain carpets can emit chemicals that can cause sensory irritation, pulmonary irritation, and neurotoxicity in mice. These experiments have been replicated in an independent laboratory (Dr. Y. Alarie, personal communication). These mouse experiments support the legitimacy of the human complaints that certain carpets can cause adverse health effects in some people."

"Although chemical analysis of carpet emissions has not provided clues by which human complaints can be evaluated, the research presented here provides a simple approach by which carpet-related health issues could be investigated. Using a standardized toxicology test method combined with routine clinical observations, we found animal reactions that indicated the presence of irritants and neurotoxic chemicals."

"The general uniformity of the clinical data, in spite of the variety of test carpet ages and the absence of geographical localization of the complaint carpet sources, rules out most explanations that invoke accidental contamination of these carpets as the source of the problem."

[2] **Dionne, J.C., Soto, J.C., and Pineau, S., "Assessment of an Ultraviolet Air Sterilizer on the Incidence of Childhood Upper Respiratory Tract Infections and Day Care Centre Indoor Air Quality,"** ***Indoor Environment*** **2: 307-311, 1993 [Issue 64, Item 43]**

The authors examined the use of ultraviolet light as a means of sterilizing the air in day care centers, as ultraviolet light is thought to have a germicidal action. Reportedly, although some decreases in the number of microorganisms occurred with the air treatment, the incidence of respiratory infections in the study children did not decrease, suggesting that transmission was not airborne, but rather, occurred by other means. The authors recommend adequate ventilation for day care centers.

EXCERPTS:

"A double-blind trial was conducted to evaluate the effect of an ultraviolet air sterilizer [UVAS] in reducing the incidence of upper respiratory infections [URI] in children and the concentration of micro-organisms in 3 day-care centres [DCC] located in Montreal."

"The study was performed [in] the autumn of 1991 among young children attending 3 DCC located in the metropolitan area of Montreal. It has been documented that children under 36 months of age in day care are at high risk of developing URI, especially in autumn."

"Children exposed to UVAS experienced a 1.53 higher URI incidence rate than those who were not. However, this difference disappeared when controlling for the age of the children."

"In rooms A and B, there was a significant reduction in airborne bacteria after the installation of the room air sterilizer. The results for rooms C and D indicate no significant reduction."

"Before and after installation of the appliances, the indoor concentrations of fungal spores were higher than those outdoors (particularly in rooms A and C). There was no significant reduction in the counts after installation of the room air sterilizers, and, surprisingly, there was a lower fungal concentration in rooms where the UV lamps were off (rooms C and D, at 3 weeks)."

"The present study showed that the efficiency of UVAS in reducing the density of airborne micro-organisms was inadequate in reducing illness in the subjects."

"Important factors that would not be controlled by UVAS include transmission by aerosol or dust and direct contamination from human contact (both children and personnel) during daily activities."

"UVAS does not offer protection against URIs, particularly in young children attending DCC. Moreover, the devices have little effect on the environmental concentration of micro-organisms. The best available measure to improve indoor air quality, which is also the least expensive, is by adequate ventilation, thus diluting any contaminants with outdoor air."

"In DCC, other routes of infection are probably most important and only a comprehensive public health programme can reduce the risk of infection and disease."

[3] **Hedge, A., Mitchell, G.E., McCarthy, J., and Ludwig, J., "The Effects of Breathing-Zone Filtration on Perceived Indoor Air Quality and Sick Building Syndrome." In:** ***Building Design, Technology, and Occupant Well-Being in Temperate Climates.*** **E. Sterling, C. Bieva, and C. Collett (eds.). Atlanta, American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc., 145-150, 1993 [Issue 65, Item 35]**

This article proposes that a breathing-zone filtration (BZF) system, which draws in "aged" air at head height, filters it and supplies "clean" air above head level, is an effective, economical supplement to the standard ventilation system. The BZF system reportedly reduced the levels of airborne particulates, and improved occupant reports of indoor air quality, symptoms, and productivity.